



FT	Misc-difference	11	/Label= OTHER
FT	/note= "Other= His or halo-His"		
FT	Misc-difference	18	/Label= OTHER
FT	/note= "Other= Arg, homoaArg, ornithine, Lys,		
FT	N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys,		
FT	any synthetic basic amino acid, His or halo-His"		
FT	Misc-difference	19	/Label= OTHER
FT	/note= "Other= Arg, homoaArg, ornithine, Lys,		
FT	N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys,		
FT	any synthetic basic amino acid, His or halo-His"		
FT	Misc-difference	22	/Label= OTHER
FT	/note= "Other= Arg, homoaArg, ornithine, Lys,		
FT	N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys,		
FT	any synthetic basic amino acid, His or halo-His"		
FT	Misc-difference	23	/Label= OTHER
FT	/note= "Other= Phe, Tyr, meta-Tyr, ortho-Tyr,		
FT	nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,		
FT	O-phospho-Tyr, nitro-Tyr, (D,L)-TTP, neo-TTP or		
FT	(D,L)-halo-TTP"		
FT	Misc-difference	25	/Label= OTHER
FT	/note= "Other= Arg, homoaArg, ornithine, Lys,		
FT	N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys,		
FT	any synthetic basic amino acid, His or halo-His"		
FT	Modified-site	27	/note= "The C-terminus is either a carboxyl group
FT	or an amide group"		
XX	WO200121648-A1.		
PN	29-MAR-2001.		
PD			
XX	21-SEP-2000: 2000WO-US25827.		
PF			
XX	22-SEP-1999: 99US-155135P.		
PR	20-JUL-2000; 2000US-0219438.		
XX			
PA	(COGN-) COGENETIX INC.		
XX			
PI	Cornelli-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;		
PI	Jones RP;		
DR	WPI; 2001-648090/74.		
XX			
PT	Treating disorders associated with radical depolarization of excitable		
PT	membrane e.g. cardiac, cerebral and ocular ischemia and asthma		
PT	comprises activating a KATP channel by administering to an individual a		
PT	kappa-conotoxin PVIIA peptide -		
XX			
PS	Claim 1; Page 27; 46pp; English.		
XX			
CC	The invention relates to treating disorders associated with radical		
CC	depolarisation of excitable membrane by activating a KATP channel		
CC	comprising administering to an individual a kappa-conotoxin PVIIA		
CC	(kappa-PVIIA) peptide or its analogue, derivative or physiologically		
CC	active salt. The conotoxins are used for treating disorders associated		
CC	with radical depolarisation of excitable membrane by activating a KATP		
CC	channel, especially cardiac ischemia, cerebral ischemia, ocular		
CC	ischemia and asthma. The present sequence is a kappa-conotoxin		
CC	PVIIA analogue of the invention.		
SQ			
	Sequence 27 AA:		
	Query Match 100.0%; Score 120; DB 22; Length 27;		
	Best Local Similarity 100.0%; Pred. NO.0.00036;		
	Matches 27; Conservative 0; Mismatches 0; Indels 0; Gaps 0;		
Y	1 CXJINOXCXOXLDDCCSXKXNXCVCV 27		

Db 1 CXTXNKCXQXLDCCSXXCNXNKCXV 27

RESULT 3  
AAU0196  
ID AAU0196 standard; peptide: 27 AA.

AC AAU0196;

DT 16-JAN-2002 (first entry)

DE Snail kappa-conotoxin PVIIA analogue R18A.

KM Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;  
cardioactive; antihistaminic; KATP channel activation; cardiac ischaemia;  
cerebral ischaemia; ocular ischaemia; asthma; R18A.

OS Conus purpurascens.  
XX Synthetic.

FT Key Location/Qualifiers

FT Modified-site 4 /note= "Hydroxyproline"

FT Modified-site 27 /note= "The C-terminus is either a carboxyl group  
or an amide group"

PN W0200121648-A1.

PD 29-MAR-2001.

PF 21-SEP-2000; 2000MO-US25827.

PR 22-SEP-1999; 99US-155135P.

PR 20-JUL-2000; 2000US-0219438.

PA (COGN-) COGNETIX INC.

XX

PI Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;

PI Jones RR;

XX

DR WPI; 2001-648090/74.

XX

PT Treating disorders associated with radical depolarization of excitable

PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma

PT comprises activating a KATP channel by administering to an individual a

PT kappa-conotoxin PVIIA peptide -

XX

PS Claim 1; Page 27; 46pp; English.

XX

CC The invention relates to treating disorders associated with radical

CC depolarisation of excitable membrane by activating a KATP channel

CC comprising administering to an individual a kappa-conotoxin PVIIA

CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically

CC active salt. The conotoxins are used for treating disorders associated

CC with radical depolarisation of excitable membrane by activating a KATP

CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular

CC ischaemia and asthma. The present sequence is a kappa-conotoxin

CC PVIIA analogue of the invention.

CC

XX

SO Sequence 27 AA;

Query Match 100.0%; Score 120; DB 22; Length 27;

Best Local Similarity 66.7%; Pred. No. 0.00036;

Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;

OY 1 CXTXNKCXQXLDCCSXXCNXNKCXV 27

DB 1 CXTXNKCXQXLDCCSXXCNXNKCXV 27

AC

XX

RESULT 4

AAU0197  
ID AAU0197 standard; peptide: 27 AA.

AC AAU0197;

DT 16-JAN-2002 (first entry)

DE Snail Kappa-conotoxin PVIIA analogue R22A.

KM Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;  
cardioactive; antihistaminic; KATP channel activation; cardiac ischaemia;  
cerebral ischaemia; ocular ischaemia; asthma; R22A.

OS Conus purpurascens.  
XX Synthetic.

FT Key Location/Qualifiers

FT Modified-site 4 /note= "Hydroxyproline"

FT Modified-site 27 /note= "The C-terminus is either a carboxyl group  
or an amide group"

PN W0200121648-A1.

PD 29-MAR-2001.

PF 21-SEP-2000; 2000MO-US25827.

PR 22-SEP-1999; 99US-155135P.

PR 20-JUL-2000; 2000US-0219438.

PA (COGN-) COGNETIX INC.

XX

PI Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;

PI Jones RR;

XX

DR WPI; 2001-648090/74.

XX

PT Treating disorders associated with radical depolarization of excitable

PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma

PT comprises activating a KATP channel by administering to an individual a

PT kappa-conotoxin PVIIA peptide -

XX

PS Claim 1; Page 27; 46pp; English.

XX

CC The invention relates to treating disorders associated with radical

CC depolarisation of excitable membrane by activating a KATP channel

CC comprising administering to an individual a kappa-conotoxin PVIIA

CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically

CC active salt. The conotoxins are used for treating disorders associated

CC with radical depolarisation of excitable membrane by activating a KATP

CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular

CC ischaemia and asthma. The present sequence is a kappa-conotoxin

CC PVIIA analogue of the invention.

CC

XX

SO Sequence 27 AA;

Query Match 100.0%; Score 120; DB 22; Length 27;

Best Local Similarity 66.7%; Pred. No. 0.00036;

Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;

OY 1 CXTXNKCXQXLDCCSXXCNXNKCXV 27

DB 1 CXTXNKCXQXLDCCSXXCNXNKCXV 27

AC

XX

RESULT 5

AAU0199

ID AAU0199 standard; peptide: 27 AA.

AC

XX

AAU0199;

XX





XX Key Location/Qualifiers  
 FT Modified-site 4 /note="Hydroxyproline"  
 FT Modified-site 27 /note="The C-terminus is either a carboxyl group  
 FT or an amide group"  
 XX  
 XX WO200121648-A1.  
 PN  
 PD 29-MAR-2001.  
 XX  
 XX 21-SEP-2000; 2000WO-US25827.  
 XX  
 XX 22-SEP-1999; 99US-155135P.  
 PR 20-JUL-2000; 2000US-0219438.  
 XX  
 XX (COGN-) COGNETIX INC.  
 PA  
 PI Corneli-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
 PI Jones RR;  
 XX  
 XX WPI; 2001-648090/74.  
 DR  
 XX Treating disorders associated with radical depolarization of excitable  
 PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma  
 PT comprises activating a KATP channel by administering to an individual a  
 PT kappa-conotoxin PVIIA peptide -  
 XX  
 XX Claim 1; Page 27; 46pp; English.  
 PS  
 CC The invention relates to treating disorders associated with radical  
 CC depolarisation of excitable membrane by activating a KATP channel  
 CC comprising administering to an individual a kappa-conotoxin PVIIA  
 CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
 CC active salt. The conotoxins are used for treating disorders associated  
 CC with radical depolarisation of excitable membrane by activating a KATP  
 CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular  
 CC ischaemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.  
 CC  
 XX  
 SQ Sequence 27 AA;  
 Query Match 100.0%; Score 120; DB 22; Length 27;  
 Best Local Similarity 66.7%; Pred. No. 0.00036;  
 Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 CXTXNCKXOHLDCCSRKXNKNXCV 27  
 DB 1 CXTXNCKXOHLDCCSRKXNKNXCV 27  
 RESULT 8  
 AAU10202  
 ID AAU10202 standard; peptide; 27 AA.  
 XX  
 AC AAU10202;  
 XX  
 DT 16-JAN-2002 (first entry)  
 XX  
 XX Snail Kappa-conotoxin PVIIA analogue K25A.  
 DE  
 XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;  
 KW cardioactive; antiaesthetic; KATP channel activation; cardiac ischaemia;  
 KW cerebral ischaemia; ocular ischaemia; asthma; K25A.  
 XX  
 OS Conus purpurascens.  
 OS Synthetic.  
 XX  
 XX Key Location/Qualifiers  
 FT Modified-site 4 /note="Hydroxyproline"  
 FT Modified-site 27 /note="The C-terminus is either a carboxyl group  
 FT or an amide group"

FT /note="The C-terminus is either a carboxyl group  
 FT or an amide group"  
 XX  
 XX WO200121648-A1.  
 PN  
 PD 29-MAR-2001.  
 XX  
 XX 21-SEP-2000; 2000WO-US25827.  
 XX  
 XX 22-SEP-1999; 99US-155135P.  
 PR 20-JUL-2000; 2000US-0219438.  
 XX  
 XX (COGN-) COGNETIX INC.  
 PA  
 PI Corneli-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
 PI Jones RR;  
 XX  
 XX WPI; 2001-648090/74.  
 DR  
 XX Treating disorders associated with radical depolarization of excitable  
 PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma  
 PT comprises activating a KATP channel by administering to an individual a  
 PT kappa-conotoxin PVIIA peptide -  
 XX  
 XX Claim 1; Page 27; 46pp; English.  
 PS  
 CC The invention relates to treating disorders associated with radical  
 CC depolarisation of excitable membrane by activating a KATP channel  
 CC comprising administering to an individual a kappa-conotoxin PVIIA  
 CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
 CC active salt. The conotoxins are used for treating disorders associated  
 CC with radical depolarisation of excitable membrane by activating a KATP  
 CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular  
 CC ischaemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.  
 CC  
 XX  
 SQ Sequence 27 AA;  
 Query Match 100.0%; Score 120; DB 22; Length 27;  
 Best Local Similarity 66.7%; Pred. No. 0.00036;  
 Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 CXTXNCKXOHLDCCSRKXNKNXCV 27  
 DB 1 CXTXNCKXOHLDCCSRKXNKNXCV 27  
 RESULT 9  
 AAU10203  
 ID AAU10203 standard; peptide; 27 AA.  
 XX  
 AC AAU10203;  
 XX  
 DT 16-JAN-2002 (first entry)  
 XX  
 XX Snail Kappa-conotoxin PVIIA analogue R2K.  
 DE  
 XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;  
 KW cardioactive; antiaesthetic; KATP channel activation; cardiac ischaemia;  
 KW cerebral ischaemia; ocular ischaemia; asthma; R2K.  
 XX  
 OS Conus purpurascens.  
 OS Synthetic.  
 XX  
 XX Key Location/Qualifiers  
 FT Modified-site 4 /note="Hydroxyproline"  
 FT Modified-site 27 /note="The C-terminus is either a carboxyl group  
 FT or an amide group"  
 XX  
 XX WO200121648-A1.

PD 29-MAR-2001.  
XX  
XX 21-SEP-2000; 2000MO-US25827.  
XX  
XX 22-SEP-1999; 99US-155135P.  
PR 20-JUL-2000; 2000US-0219438.  
XX  
XX (COGN-) COGNETIX INC.  
XX  
XX Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
PI Jones RR;  
DR WPI: 2001-648090/74.  
XX  
XX Treating disorders associated with radical depolarization of excitable  
PT membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
PT comprises activating a KATP channel by administering to an individual a  
PT kappa-conotoxin PVIIA peptide -  
XX  
XX Claim 1; Page 27; 46pp; English.  
XX  
XX The invention relates to treating disorders associated with radical  
CC depolarisation of excitable membrane by activating a KATP channel  
CC comprising administering to an individual a kappa-conotoxin PVIIA  
CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
CC active salt. The conotoxins are used for treating disorders associated  
CC with radical depolarisation of excitable membrane by activating a KATP  
CC channel, especially cardiac ischemia, cerebral ischemia, ocular  
CC ischemia and asthma. The present sequence is a kappa-conotoxin  
CC PVIIA analogue of the invention.  
XX  
XX Sequence 27 AA;  
SQ  
Query Match 100.0%; Score 120; DB 22; Length 27;  
Best Local Similarity 66.7%; Pred. No. 0.00036;  
Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;  
OY 1 CXINQXQXLDCCSXKXNXXCV 27  
DB 1 CXINQXQXLDCCSXKXNXXCV 27  
RESULT 10  
AAU10204  
ID AAU10204 standard; peptide: 27 AA.  
XX  
XX AAU10204;  
AC  
XX 16-JAN-2002 (first entry)  
DT  
XX  
XX Snail Kappa-conotoxin PVIIA analogue K7A.  
DE  
XX  
XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;  
KW cardioactive; antihistaminic; KATP channel activation; cardiac ischemia;  
KW cerebral ischemia; ocular ischemia; asthma; K7A.  
XX  
XX Conus purpurascens.  
OS Synthetic.  
OS  
XX  
XX Key Location/Qualifiers  
FH Modified-site 4 /note= "Hydroxyproline"  
FT  
FT Modified-site 27 /note= "The C-terminus is either a carboxyl group  
FT or an amide group"  
FT  
XX  
XX WO200121648-A1.  
PN  
XX  
XX 29-MAR-2001.  
PD  
XX  
XX 21-SEP-2000; 2000MO-US25827.  
PR  
XX  
XX 22-SEP-1999; 99US-155135P.

PR 20-JUL-2000; 2000US-0219438.  
XX  
XX (COGN-) COGNETIX INC.  
XX  
XX Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
PI Jones RR;  
DR WPI: 2001-648090/74.  
XX  
XX Treating disorders associated with radical depolarization of excitable  
PT membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
PT comprises activating a KATP channel by administering to an individual a  
PT kappa-conotoxin PVIIA peptide -  
XX  
XX Claim 1; Page 28; 46pp; English.  
XX  
XX The invention relates to treating disorders associated with radical  
CC depolarisation of excitable membrane by activating a KATP channel  
CC comprising administering to an individual a kappa-conotoxin PVIIA  
CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
CC active salt. The conotoxins are used for treating disorders associated  
CC with radical depolarisation of excitable membrane by activating a KATP  
CC channel, especially cardiac ischemia, cerebral ischemia, ocular  
CC ischemia and asthma. The present sequence is a kappa-conotoxin  
CC PVIIA analogue of the invention.  
XX  
XX Sequence 27 AA;  
SQ  
Query Match 100.0%; Score 120; DB 22; Length 27;  
Best Local Similarity 66.7%; Pred. No. 0.00036;  
Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;  
OY 1 CXINQXQXLDCCSXKXNXXCV 27  
DB 1 CXINQXQXLDCCSXKXNXXCV 27  
RESULT 11  
AAU10205  
ID AAU10205 standard; peptide: 27 AA.  
XX  
XX AAU10205;  
AC  
XX 16-JAN-2002 (first entry)  
DT  
XX  
XX Snail Kappa-conotoxin PVIIA analogue P9M.  
DE  
XX  
XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;  
KW cardioactive; antihistaminic; KATP channel activation; cardiac ischemia;  
KW cerebral ischemia; ocular ischemia; asthma; P9M.  
XX  
XX Conus purpurascens.  
OS Synthetic.  
OS  
XX  
XX Key Location/Qualifiers  
FH Modified-site 4 /note= "Hydroxyproline"  
FT  
FT Modified-site 27 /note= "The C-terminus is either a carboxyl group  
FT or an amide group"  
FT  
XX  
XX WO200121648-A1.  
PN  
XX  
XX 29-MAR-2001.  
PD  
XX  
XX 21-SEP-2000; 2000MO-US25827.  
PR  
XX  
XX 22-SEP-1999; 99US-155135P.  
PR 20-JUL-2000; 2000US-0219438.  
XX  
XX (COGN-) COGNETIX INC.  
XX  
XX Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;

PI Jones RR;  
XX WPI: 2001-648090/74.

PT Treating disorders associated with radical depolarization of excitable  
DR membrane e.g. cardiac, cerebral and ocular ischaemia and asthma  
XX comprises activating a KATP channel by administering to an individual a  
PT kappa-conotoxin PVIIA peptide -  
PS Claim 1; Page 28; 46pp; English.

XX The invention relates to treating disorders associated with radical  
CC depolarisation of excitable membrane by activating a KATP channel  
CC comprising administering to an individual a kappa-conotoxin PVIIA  
CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
CC active salt. The conotoxins are used for treating disorders associated  
CC with radical depolarisation of excitable membrane by activating a KATP  
CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular  
CC ischaemia and asthma. The present sequence is a kappa-conotoxin  
CC PVIIA analogue of the invention.

SQ Sequence 27 AA;

Query Match 100.0%; Score 120; DB 22; Length 27;  
Best Local Similarity 66.7%; Pred. No. 0.00036;  
Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;

OY 1 CXIXNQCXQXLDCCSXKCNXNXCVCV 27  
1:|||||:|:|||||:|:|||||  
DB 1 CRIXNQCXQXLDCCSXKCNXNXCVCV 27

RESULT 12

AAU10206 standard; peptide; 27 AA.

AC AAU10206;

DT 16-JAN-2002 (first entry)

XX Small Kappa-conotoxin PVIIA analogue F9Y.

XX Purple cone snail; Kappa-conotoxin PVIIA analogue; circulatory;

KW cardioactive; antiasthmatic; KATP channel activation; cardiac ischaemia;

XX cerebral ischaemia; ocular ischaemia; asthma; F9Y.

OS Conus purpurascens.

OS Synthetic.

FT Key Location/Qualifiers  
FT Modified-site 4 /note= "Hydroxyproline"  
FT Modified-site 27 /note= "The C-terminus is either a carboxyl group  
or an amide group"

XX WO200121648-A1.

PD 29-MAR-2001.

PF 21-SEP-2000; 2000WO-US25827.

XX 22-SEP-1999; 99US-155135P.

PR 20-JUL-2000; 2000US-0219438.

XX (COGN-) COGNETIX INC.

XX Corneli-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;

XX Jones RR;  
XX WPI: 2001-648090/74.

PT Treating disorders associated with radical depolarization of excitable

PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma  
XX comprises activating a KATP channel by administering to an individual a  
PT kappa-conotoxin PVIIA peptide -

PS Claim 1; Page 28; 46pp; English.

XX The invention relates to treating disorders associated with radical  
CC depolarisation of excitable membrane by activating a KATP channel  
CC comprising administering to an individual a kappa-conotoxin PVIIA  
CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
CC active salt. The conotoxins are used for treating disorders associated  
CC with radical depolarisation of excitable membrane by activating a KATP  
CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular  
CC ischaemia and asthma. The present sequence is a kappa-conotoxin  
CC PVIIA analogue of the invention.

SQ Sequence 27 AA;

Query Match 100.0%; Score 120; DB 22; Length 27;  
Best Local Similarity 66.7%; Pred. No. 0.00036;  
Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;

OY 1 CXIXNQCXQXLDCCSXKCNXNXCVCV 27  
1:|||||:|:|||||:|:|||||  
DB 1 CRIXNQCXQXLDCCSXKCNXNXCVCV 27

RESULT 13

AAU10207 standard; peptide; 27 AA.

AC AAU10207;

DT 16-JAN-2002 (first entry)

XX Small Kappa-conotoxin PVIIA analogue R2Q.

XX Purple cone snail; Kappa-conotoxin PVIIA analogue; circulatory;

KW cardioactive; antiasthmatic; KATP channel activation; cardiac ischaemia;

XX cerebral ischaemia; ocular ischaemia; asthma; R2Q.

OS Conus purpurascens.

OS Synthetic.

FT Key Location/Qualifiers  
FT Modified-site 4 /note= "Hydroxyproline"  
FT Modified-site 27 /note= "The C-terminus is either a carboxyl group  
or an amide group"

XX WO200121648-A1.

PD 29-MAR-2001.

PF 21-SEP-2000; 2000WO-US25827.

XX 22-SEP-1999; 99US-155135P.

PR 20-JUL-2000; 2000US-0219438.

XX (COGN-) COGNETIX INC.

XX Corneli-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;

XX Jones RR;  
XX WPI: 2001-648090/74.

PT Treating disorders associated with radical depolarization of excitable  
PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma  
PT comprises activating a KATP channel by administering to an individual a  
PT kappa-conotoxin PVIIA peptide -

PS Claim 1; Page 28; 46pp; English.

XX The invention relates to treating disorders associated with radical  
 CC depolarisation of excitable membrane by activating a KARP channel  
 CC comprising administering to an individual a kappa-conotoxin PVIIA  
 CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
 CC active salt. The conotoxins are used for treating disorders associated  
 CC with radical depolarisation of excitable membrane by activating a KARP  
 CC channel, especially cardiac ischemia, cerebral ischemia, ocular  
 CC ischemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.  
 XX  
 SQ Sequence 27 AA:

Query Match 100.0%; Score 120; DB 22; Length 27;  
 Best Local Similarity 66.7%; Pred. No. 0.00036;  
 Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;

QY 1 CXINQXCXQXLDCCSXKCNKXKCV 27  
 DB 1 COIXNKCXQXLDCCSRKCNKXKCV 27

## RESULT 14

AAU10208 standard; peptide: 27 AA.

AC AAU10208;

DT 16-JAN-2002 (first entry)

DE Snail Kappa-conotoxin PVIIA analogue H1A.

XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;

KW cardioactive; antisthmatic; KARP channel activation; cardiac ischemia;

KW cerebral ischemia; ocular ischemia; asthma; H1A.

XX Conus purpurascens.

OS Synthetic.

PH Key Location/Qualifiers

FT Modified-site 4 /note= "Hydroxyproline"

FT Modified-site 27 /note= "The C-terminus is either a carboxyl group

FT or an amide group"

XX WO200121648-A1.

XX 29-MAR-2001.

XX 21-SEP-2000; 2000WO-US25827.

XX 22-SEP-1999; 99US-155135P.

XX 20-JUL-2000; 2000US-0219438.

XX (COGN-) COGNETIX INC.

XX Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;

PI Jones RR;

XX WPI; 2001-648090/74.

PT Treating disorders associated with radical depolarization of excitable  
 PT membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
 PT comprises administering to an individual a kappa-conotoxin PVIIA  
 PT kappa-conotoxin PVIIA peptide -  
 XX Claim 1; Page 28; 46pp; English.

CC The invention relates to treating disorders associated with radical  
 CC depolarisation of excitable membrane by activating a KARP channel  
 CC comprising administering to an individual a kappa-conotoxin PVIIA  
 CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically

CC active salt. The conotoxins are used for treating disorders associated  
 CC with radical depolarisation of excitable membrane by activating a KARP  
 CC channel, especially cardiac ischemia, cerebral ischemia, ocular  
 CC ischemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.  
 XX  
 SQ Sequence 27 AA:

Query Match 100.0%; Score 120; DB 22; Length 27;  
 Best Local Similarity 66.7%; Pred. No. 0.00036;  
 Matches 18; Conservative 9; Mismatches 0; Indels 0; Gaps 0;

QY 1 CXINQXCXQXLDCCSXKCNKXKCV 27  
 DB 1 COIXNKCXQXLDCCSRKCNKXKCV 27

## RESULT 15

AAU10218 standard; peptide: 27 AA.

AC AAU10218;

DT 16-JAN-2002 (first entry)

DE Snail Kappa-conotoxin PVIIA analogue Q4A.

XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;

KW cardioactive; antisthmatic; KARP channel activation; cardiac ischemia;

KW cerebral ischemia; ocular ischemia; asthma; Q4A.

XX Conus purpurascens.

OS Synthetic.

PH Key Location/Qualifiers

FT Modified-site 4 /note= "Hydroxyproline"

FT Modified-site 27 /note= "The C-terminus is either a carboxyl group

FT or an amide group"

XX WO200121648-A1.

XX 29-MAR-2001.

XX 21-SEP-2000; 2000WO-US25827.

XX 22-SEP-1999; 99US-155135P.

XX 20-JUL-2000; 2000US-0219438.

XX (COGN-) COGNETIX INC.

XX Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;

PI Jones RR;

XX WPI; 2001-648090/74.

PT Treating disorders associated with radical depolarization of excitable  
 PT membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
 PT comprises administering to an individual a kappa-conotoxin PVIIA  
 PT kappa-conotoxin PVIIA peptide -  
 XX Claim 1; Page 28; 46pp; English.

CC The invention relates to treating disorders associated with radical  
 CC depolarisation of excitable membrane by activating a KARP channel  
 CC comprising administering to an individual a kappa-conotoxin PVIIA  
 CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
 CC active salt. The conotoxins are used for treating disorders associated  
 CC with radical depolarisation of excitable membrane by activating a KARP  
 CC channel, especially cardiac ischemia, cerebral ischemia, ocular  
 CC ischemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.

XX	Sequence	27	AA;
SQ			

Query Match	100.0%	Score 120;	DB 22;	Length 27;
Best Local Similarity	63.0%;	Pred. No. 0.00336;		
Matches 17;	Conservative 10;	Mismatches 0;	Indels 0;	Gaps 0;

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Db 1 CRIANQKCFQHLDDCCSRKCNRFNKCV 27
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Search completed: January 14, 2003, 18:30:46  
Job time : 36 secs

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GenCore version 5.1.3  
Copyright (c) 1993 - 2003 Comugen Ltd.

OM protein - protein search, using sw model

Run on: January 14, 2003, 18:30:11 ; Search time 14 Seconds  
(without alignments)  
56.744 Million cell updates/sec

Title: US-09-666-837B-1

Perfect score: 120  
Sequence: 1 CXIXNQXCXQXLDCCSXCNXNCV 27

Scoring table:  
Gapop 10.0 , Gapext 0.5

Searched: 262574 seqs, 2942292 residues

Total number of hits satisfying chosen parameters: 262574

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database :

Issued\_Patents\_Aa: \*  
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3: /cgn2\_6/ptodata/1/1aa/6A.COMB.pep: \*  
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pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

#### SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
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3	81	67.5	26	1	US-08-049-794-19
4	81	67.5	26	1	US-08-496-847-19
5	81	67.5	26	2	US-08-742-774-19
6	81	67.5	26	2	US-08-673-354-19
7	81	67.5	26	2	US-08-965-918-19
8	81	67.5	26	2	US-09-138-439-19
9	81	67.5	26	3	US-08-613-400A-19
10	81	67.5	26	3	US-09-298-017-19
11	81	67.5	26	4	US-09-392-979A-19
12	77	64.2	26	1	US-07-789-913-8
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15	77	64.2	26	2	US-08-742-774-8
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19	77	64.2	26	3	US-08-613-400A-8
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21	77	64.2	26	4	US-09-392-979A-8
22	72	60.0	2523	4	US-08-185-432-18
23	72	60.0	2523	4	US-08-899-232-3
24	69	57.5	26	1	US-08-049-794-21
25	69	57.5	26	1	US-08-049-794-29
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27	69	57.5	26	1	US-08-496-847-29

28	69	57.5	26	2	US-08-742-774-21	Sequence 21, Appl
29	69	57.5	26	2	US-08-742-774-29	Sequence 29, Appl
30	69	57.5	26	2	US-08-675-354-21	Sequence 21, Appl
31	69	57.5	26	2	US-08-675-354-29	Sequence 29, Appl
32	69	57.5	26	2	US-08-965-918-21	Sequence 21, Appl
33	69	57.5	26	2	US-08-965-918-29	Sequence 29, Appl
34	69	57.5	26	2	US-09-138-439-21	Sequence 21, Appl
35	69	57.5	26	2	US-09-138-439-29	Sequence 29, Appl
36	69	57.5	26	3	US-08-613-400A-21	Sequence 21, Appl
37	69	57.5	26	3	US-08-613-400A-29	Sequence 29, Appl
38	69	57.5	26	3	US-09-298-017-21	Sequence 21, Appl
39	69	57.5	26	3	US-09-298-017-29	Sequence 29, Appl
40	69	57.5	26	4	US-09-392-979A-21	Sequence 21, Appl
41	69	57.5	26	4	US-09-392-979A-29	Sequence 29, Appl
42	69	57.5	29	1	US-08-092-215-9	Sequence 9, Appl
43	68	56.7	2556	1	US-08-185-432-17	Sequence 17, Appl
44	68	56.7	2556	1	US-08-083-590A-20	Sequence 20, Appl
45	68	56.7	2556	3	US-08-532-384-20	Sequence 20, Appl

#### ALIGNMENTS

RESULT 1  
US-08-619-936-1  
Sequence 1, Application US/08619936  
Patent No. 5672682  
GENERAL INFORMATION:  
APPLICANT: Terlau, Heinrich  
APPLICANT: Shon, Ki-Joon  
APPLICANT: Grille, Michelle  
APPLICANT: Olivera, Baldoiero M.  
TITLE OF INVENTION: Conotoxin Peptide PVIIA  
NUMBER OF SEQUENCES: 1  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Venable, Baetjer, Howard & Civiletti, LLP  
STREET: 1201 New York Avenue, Suite 1000  
CITY: Washington  
STATE: DC  
COUNTRY: U.S.A.  
ZIP: 20005  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: Patent Release #1.0, Version #1.30  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/619,936  
CLASSIFICATION: 530  
ATTORNEY/AGENT INFORMATION:  
NAME: Saxe, Stephen A.  
REGISTRATION NUMBER: 38,609  
REFERENCE/DOCKET NUMBER: 24260-107674-04  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: 202-962-4848  
TELEFAX: 202-962-8300  
INFORMATION FOR SEQ ID NO: 1:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 27 amino acids  
TYPE: amino acid  
STRANDEDNESS: single  
TOPOLOGY: linear  
MOLECULE TYPE: peptide  
HYDROTHERICAL: NO  
ORIGINAL SOURCE:  
ORGANISM: Conus purpurascens  
FEATURE:  
NAME/KEY: Modified-site  
LOCATION: 4  
OTHER INFORMATION: /product= "4Hyp"  
OTHER INFORMATION: /note= "Amino acid 4 may be 4-trans-hydroxyproline."  
FEATURE:





GENERAL INFORMATION:  
APPLICANT: Amstutz, Gary A.  
APPLICANT: Howersox, Stephen S.  
APPLICANT: Gohil, Kishorchandra  
APPLICANT: Adriaenssens, Peter I.  
APPLICANT: Kristipati, Ramasharma  
TITLE OF INVENTION: METHODS AND  
TITLE OF INVENTION: FORMULATIONS FOR PREVENTING PROGRESSION OF NEUROPATHIC PAIN  
NUMBER OF SEQUENCES: 36  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Dehlinger & Associates  
STREET: 350 Cambridge Avenue, Suite 250  
CITY: Palo Alto  
STATE: CA  
COUNTRY: US  
ZIP: 94306-1546  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Diskette  
COMPUTER: IBM Compatible  
OPERATING SYSTEM: DOS  
SOFTWARE: FastSeq for Windows Version 2.0  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/496,847  
FILING DATE: 27-JUN-1995  
CLASSIFICATION: 514  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0009.31  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: 650-324-0960  
TELEFAX: 650-324-0960  
INFORMATION FOR SEQ ID NO: 19:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: amino acid  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHEICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-08-496-847-19  
Query Match 67.5%; Score 81; DB 1; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.14;  
Matches 9; Conservative 13; Mismatches 4; Indels 0; Gaps 0;  
QY 1 CXINQXQXLDCCSXKXNXXNC 26  
Db 1 CKLKGSCSRIMYDCCSGSGRSGKC 26  
RESULT 5  
US-08-742-774-19  
Sequence 19, Application US/08742774  
Patent No. 5824645  
GENERAL INFORMATION:  
APPLICANT: JUSTICE, ALAN  
APPLICANT: SINGH, TEJINDER  
APPLICANT: GOHIL, KISHOR C  
APPLICANT: VALENTINO, KAREN L  
APPLICANT: MILJANICH, GEORGE P  
TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
TITLE OF INVENTION: ENHANCING OPIATE ANALGESIA  
NUMBER OF SEQUENCES: 34  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:

MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: PatentIn Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/742,774  
FILING DATE:  
CLASSIFICATION:  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: 08/675,354  
FILING DATE: 03-JUL-1996  
APPLICATION NUMBER: US/08/049,794  
FILING DATE: 1993-APR-15  
APPLICATION NUMBER: US 07/814,759  
FILING DATE: 30-DEC-1991  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0009.30  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: (415) 324-0880  
TELEFAX: (415) 324-0960  
INFORMATION FOR SEQ ID NO: 19:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: amino acid  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHEICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-08-742-774-19  
Query Match 67.5%; Score 81; DB 2; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.14;  
Matches 9; Conservative 13; Mismatches 4; Indels 0; Gaps 0;  
QY 1 CXINQXQXLDCCSXKXNXXNC 26  
Db 1 CKLKGSCSRIMYDCCSGSGRSGKC 26  
RESULT 6  
US-08-675-354-19  
Sequence 19, Application US/08675354  
Patent No. 5859186  
GENERAL INFORMATION:  
APPLICANT: JUSTICE, ALAN  
APPLICANT: SINGH, TEJINDER  
APPLICANT: GOHIL, KISHOR C  
APPLICANT: VALENTINO, KAREN L  
APPLICANT: MILJANICH, GEORGE P  
TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
TITLE OF INVENTION: ENHANCING OPIATE ANALGESIA  
NUMBER OF SEQUENCES: 34  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: PatentIn Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/675,354  
FILING DATE: 03-JUL-1996  
CLASSIFICATION: 530  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: US/08/049,794



RESULT 9  
US-08-613-400A-19  
; Sequence 19, Application US/08613400A  
; Patent No. 6054429  
; GENERAL INFORMATION:  
; APPLICANT: Bowersox, S. Scott  
; APPLICANT: Gadbois, Theresa  
; APPLICANT: Petrus, Mark, R.  
; APPLICANT: Luther, Robert, R.  
; TITLE OF INVENTION: IMPROVED EPIDURAL  
; TITLE OF INVENTION: METHOD OF PRODUCING ANALGESIA  
; NUMBER OF SEQUENCES: 36  
; CORRESPONDENCE ADDRESS:  
; ADDRESSEE: Dehlinger & Associates  
; STREET: 350 Cambridge Avenue, Suite 250  
; CITY: Palo Alto  
; STATE: CA  
; COUNTRY: US  
; ZIP: 94306-1546  
; COMPUTER READABLE FORM:  
; MEDIUM TYPE: Diskette  
; COMPUTER: IBM Compatible  
; OPERATING SYSTEM: DOS  
; SOFTWARE: FASTSEQ for Windows Version 2.0  
; CURRENT APPLICATION DATA:  
; APPLICATION NUMBER: US/08/613,400A  
; FILING DATE: 08-MAR-1996  
; CLASSIFICATION: 514  
; PRIOR APPLICATION DATA:  
; APPLICATION NUMBER:  
; FILING DATE:  
; ATTORNEY/AGENT INFORMATION:  
; NAME: Stratford, Carol A  
; REGISTRATION NUMBER: 34,444  
; TELECOMMUNICATION INFORMATION:  
; TELEPHONE: 650-324-0880  
; TELEFAX: 650-324-0960  
; INFORMATION FOR SEQ ID NO: 19:  
; SEQUENCE CHARACTERISTICS:  
; LENGTH: 26 amino acids  
; TYPE: amino acid  
; TOPOLOGY: linear  
; MOLECULE TYPE: protein  
; HYPOTHEICAL: NO  
; ORIGINAL SOURCE:  
; INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-08-613-400A-19  
Query Match 67.5%; Score 81; DB 3; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.14;  
Matches 9; Conservative 13; Mismatches 4; Indels 0; Gaps 0;  
DB 1 CXLKGGSCSRIMTDCCGSGGSGRSGKC 26

ADDRESSSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: PatentIn Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
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FILING DATE:  
CLASSIFICATION:  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: 08/049,794  
FILING DATE:  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0009.30  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: (415) 324-0880  
TELEFAX: (415) 324-0960  
INFORMATION FOR SEQ ID NO: 19:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: amino acid  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHEICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-09-298-017-19  
Query Match 67.5%; Score 81; DB 3; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.14;  
Matches 9; Conservative 13; Mismatches 4; Indels 0; Gaps 0;  
DB 1 CXLKGGSCSRIMTDCCGSGGSGRSGKC 26

RESULT 11  
US-09-392-979A-19  
; Sequence 19, Application US/09392979A  
; Patent No. 6136786  
; GENERAL INFORMATION:  
; APPLICANT: JUSTICE, ALAN  
; APPLICANT: SINGH, TEJINDER  
; APPLICANT: GOHIL, KISHOR C  
; APPLICANT: VALENTINO, KAREN L  
; APPLICANT: MILJANICH, GEORGE P  
; TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
; TITLE OF INVENTION: ENHANCING OPiate ANALGESIA  
; NUMBER OF SEQUENCES: 34  
; CORRESPONDENCE ADDRESS:  
; ADDRESSEE: Law Offices of Peter Dehlinger  
; STREET: 350 Cambridge Avenue, Suite 300  
; CITY: Palo Alto  
; STATE: CA  
; COUNTRY: USA  
; ZIP: 94306  
; COMPUTER READABLE FORM:  
; MEDIUM TYPE: Floppy disk  
; COMPUTER: IBM PC compatible  
; OPERATING SYSTEM: PC-DOS/MS-DOS  
; SOFTWARE: PatentIn Release #1.0, Version #1.25  
; CURRENT APPLICATION DATA:  
; APPLICATION NUMBER: US/09/392,979A  
; FILING DATE:

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1      RESULT 13
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3      ? Sequence 8, Application US/08049794
4      ? Patent No. 5587454
5      ?
6      ? GENERAL INFORMATION:
7      ? APPLICANT: JUSTICE, ALAN
8      ? APPLICANT: SINGH, TEJINDER
9      ? APPLICANT: GOHIL, KISHOR C
10     ? APPLICANT: VALENTINO, KAREN L
11     ? APPLICANT: MILANICH, GEORGE P
12     ? TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND
13     ? TITLE OF INVENTION: ENHANCING OPIATE ANALGESIA
14     ? NUMBER OF SEQUENCES: 34
15     ? CORRESPONDENCE ADDRESS:
16     ? ADDRESSEE: Law Offices of Peter Dehlinger
17     ? STREET: 350 Cambridge Avenue, Suite 300
18     ? CITY: Palo Alto
19     ? STATE: CA
20     ? COUNTRY: USA
21     ? ZIP: 94306
22     ? COMPUTER READABLE FORM:
23     ? MEDIUM TYPE: Floppy disk
24     ? COMPUTER: IBM PC compatible
25     ? OPERATING SYSTEM: PC-DOS/MS-DOS
26     ? SOFTWARE: PatentIn Release #1.0, Version #1.25
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29     ? FILING DATE: 19930415
30     ? CLASSIFICATION: 514
31     ? PRIOR APPLICATION DATA:
32     ? APPLICATION NUMBER: US 07/814,759
33     ? FILING DATE: 30-DEC-1991
34     ? ATTORNEY/AGENT INFORMATION:
35     ? NAME: Stratford, Carol A.
36     ? REGISTRATION NUMBER: 34,444
37     ? REFERENCE/DOCKET NUMBER: 5865-0009.30
38     ? TELECOMMUNICATION INFORMATION:
39     ? TELEPHONE: (415) 324-0880
40     ? TELEFAX: (415) 324-0960
41     ? INFORMATION FOR SEQ ID NO: 8:
42     ? SEQUENCE CHARACTERISTICS:
43     ? LENGTH: 26 amino acids
44     ? TYPE: AMINO ACID
45     ? TOPOLOGY: linear
46     ? MOLECULE TYPE: protein
47     ? HYPOTHEetical: NO
48     ? ORIGINAL SOURCE:
49     ? INDIVIDUAL ISOLATE: SVIB/SNX-183, FIGURE 1
50     ?
51     ? US-08-049-794-8

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GenCore version 5.1.3  
Copyright (c) 1993 - 2003 Compugen Ltd.

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Run on: January 14, 2003, 18:30:52 ; Search time 11 seconds  
(without alignments)  
47.621 Million cell updates/sec

Title: US-09-666-837B-1  
Sequence: 1 CXINQXCKXILDDCCSXCNXNXCVCV 27

Scoring table: BLOSUM62DX  
Gapop 10.0 , Gapext 0.5

Searched: 118974 seqs, 19401057 residues  
Total number of hits satisfying chosen parameters: 118974

Minimum DB seq length: 0  
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Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : Published Applications\_AA:\*

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- 2: /cgn2\_6/ptodata/2/pubpaa/PTCT\_NEW\_PUB.pep.\*
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- 14: /cgn2\_6/ptodata/2/pubpaa/US60\_PUBCOMB.pep.\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	68	56.7	2444	10 US-09-944-849-2	Sequence 2, Appl1
2	66	55.0	176	9 US-10-024-599-4	Sequence 4, Appl1
3	66	55.0	721	10 US-09-908-322-5	Sequence 5, Appl1
4	65.5	54.6	36	10 US-09-894-882-168	Sequence 168, App
5	65.5	54.6	36	10 US-09-894-882-369	Sequence 369, App
6	65.5	54.6	73	10 US-09-894-882-167	Sequence 167, App
7	64.5	53.8	32	10 US-09-894-882-364	Sequence 364, App
8	64.5	53.8	32	10 US-09-894-882-413	Sequence 413, App
9	64.5	53.8	33	10 US-09-894-882-119	Sequence 119, App
10	63.5	52.9	71	10 US-09-894-882-324	Sequence 324, App
11	63.5	52.9	36	10 US-09-894-882-339	Sequence 339, App
12	63.5	52.9	36	10 US-09-894-882-441	Sequence 441, App
13	63.5	52.9	36	10 US-09-894-882-443	Sequence 443, App
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15	63.5	52.9	72	10 US-09-894-882-338	Sequence 338, App
16	63	52.5	76	9 US-09-749-637A-207	Sequence 207, App
17	63	52.5	1055	10 US-09-855-722-2	Sequence 2, Appl1
18	63	52.5	1212	10 US-09-855-722-3	Sequence 3, Appl1
19	63	52.5	1238	10 US-09-855-722-5	Sequence 5, Appl1

20	63	52.5	1238	10 US-09-944-849-4	Sequence 4, Appl1
21	62.5	52.1	35	10 US-09-894-882-433	Sequence 433, App
22	62.5	52.1	36	10 US-09-894-882-210	Sequence 210, App
23	62.5	52.1	36	10 US-09-894-882-404	Sequence 404, App
24	62.5	52.1	70	10 US-09-894-882-209	Sequence 209, App
25	62.5	52.1	71	10 US-09-894-882-74	Sequence 74, Appl
26	62	51.7	157	10 US-09-894-882-68	Sequence 68, Appl
27	62	51.7	165	10 US-09-867-550-1550	Sequence 1550, Ap
28	62	51.7	196	10 US-09-908-322-35	Sequence 35, Appl
29	62	51.7	520	10 US-09-995-593A-3	Sequence 3, Appl1
30	62	51.7	702	10 US-09-995-593A-4	Sequence 4, Appl1
31	62	51.7	722	10 US-09-908-322-12	Sequence 12, Appl
32	62	51.7	723	9 US-10-028-072-346	Sequence 346, App
33	62	51.7	723	10 US-09-828-366-21	Sequence 21, Appl
34	62	51.7	723	10 US-09-995-593A-9	Sequence 9, Appl1
35	61.5	51.2	35	10 US-09-894-882-409	Sequence 409, App
36	61.5	51.2	36	9 US-09-814-452-25	Sequence 25, Appl
37	61.5	51.2	36	10 US-09-894-882-401	Sequence 401, App
38	61.5	51.2	36	10 US-09-894-882-403	Sequence 403, App
39	61.5	51.2	70	10 US-09-894-882-200	Sequence 200, App
40	61.5	51.2	70	10 US-09-894-882-206	Sequence 206, App
41	61.5	51.2	72	10 US-09-894-882-107	Sequence 107, App
42	61	50.8	728	10 US-09-908-322-2	Sequence 2, Appl1
43	61	50.8	1404	10 US-09-944-849-8	Sequence 8, Appl1
44	61	50.8	1480	12 US-10-011-064-5	Sequence 5, Appl1
45	61	50.8	3571	9 US-10-150-821-2	Sequence 2, Appl1

## ALIGNMENTS

RESULT 1  
US-09-944-849-2  
Sequence 2, Application US/09944849  
Patent No. US20020151487A1  
GENERAL INFORMATION:  
APPLICANT: Nickoloff, Brian  
APPLICANT: Miele, Lucio  
TITLE OF INVENTION: METHOD AND REAGENTS FOR EPITHELIAL BARRIER FORMATION AND TREAT  
TITLE OF INVENTION: MALIGNANT AND BENIGN SKIN DISORDERS BY MODULATING THE NOTCH P  
FILE REFERENCE: 212583  
CURRENT APPLICATION NUMBER: US/09/944,849  
CURRENT FILING DATE: 2001-08-31  
PRIOR APPLICATION NUMBER: US 60/229,614  
PRIOR FILING DATE: 2000-08-31  
NUMBER OF SEQ ID NOS: 18  
SOFTWARE: PatentIn version 3.1  
SEQ ID NO 2  
LENGTH: 2444  
TYPE: PRT  
ORGANISM: Artificial Sequence  
FEATURE:  
NAME/KEY: misc\_feature  
LOCATION: (691)..(691)  
OTHER INFORMATION: The 'Xaa' at location 891 stands for Gly, or Ala.  
NAME/KEY: misc\_feature  
LOCATION: (1763)..(1763)  
OTHER INFORMATION: The 'Xaa' at location 1763 stands for Gln, Arg, Pro, or Leu.  
NAME/KEY: misc\_feature  
LOCATION: (1787)..(1787)  
OTHER INFORMATION: The 'Xaa' at location 1787 stands for Thr, Ala, Pro, or Ser.  
OTHER INFORMATION: Constitutively Active No. US20020151487A1ch-1  
US-09-944-849-2

Query Match 56.7%; Score 68; DB 10; Length 2444;  
Best local Similarity 30.8%; Pred. No. 48;  
Matches 8; Conservative 12; Mismatches 6; Indels 0; Gaps 0;  
2 CXINQXCKXILDDCCSXCNXNXCVCV 27  
DB 248 GFTGQNCENIDDCGNCKNGACV 273

```

RESULT 2
US-10-024-599-4
: Sequence 4, Application US/10024599
: Patent No. US20020165352A1
: GENERAL INFORMATION:
: APPLICANT: Myriad Genetics, Inc.
: APPLICANT: Cimborra, Daniel M.
: APPLICANT: Heichman, Karen
: APPLICANT: Bartel, Paul L.
: TITLE OF INVENTION: Protein-Protein Interactions
: FILE REFERENCE: 2318-278-11
: CURRENT APPLICATION NUMBER: US/10/024,599
: PRIOR FILING DATE: 2001-12-21
: PRIOR APPLICATION NUMBER: US 60/256,986
: PRIOR FILING DATE: 2000-12-21
: NUMBER OF SEQ ID NOS: 6
: SOFTWARE: PatentIn version 3.0
: SEQ ID NO 4
: LENGTH: 176
: TYPE: PRT
: ORGANISM: Homo sapiens
: FEATURE:
: NAME/KEY: PEPTIDE
: LOCATION: 1..176
: OTHER INFORMATION: Xaa is Gly or Cys
US-10-024-599-4

Query Match          55.0%; Score 66; DB 9; Length 176;
Best Match Similarity 25.8%; Pred. No. 6,6;
Matches      8; Conservative 14; Mismatches      5; Indels      4; Gaps      1.

OY      1 CXIXN---OXCXQXLDCCSXKXKXNXCXV 27
: 1: 1 :1:::111 :1 :1:::1:
Db      9 CVCVNGMSGDDCSENIDDCAFASCTPGSYCI 39

RESULT 3
US-09-908-322-5
: Sequence 5, Application US/09908322
: Patent No. US20020107194A1
: GENERAL INFORMATION:
: APPLICANT: Ish-Horowicz, David
: Henriquez, Domingos Manuel Pinto
: Lewis, Julian Hart
: Artavanis-Tsakonas, Spyridon
: Gray, Grace
: TITLE OF INVENTION: NUCLEOTIDE AND PROTEIN SEQUENCES OF
: VERTEBRATE DELTA GENE AND METHODS BASED THEREON
: NUMBER OF SEQUENCES: 94
: CORRESPONDENCE ADDRESS:
: ADDRESSEE: Pennie & Edmonds LLP
: STREET: 1155 Avenue of the Americas
: CITY: New York
: STATE: NY
: COUNTRY: USA
: ZIP: 10036/2711
: COMPUTER READABLE FORM:
: MEDIUM TYPE: Diskette
: COMPUTER: IBM Compatible
: OPERATING SYSTEM: DOS
: SOFTWARE: FastSeq Version 2.0
: CURRENT APPLICATION DATA:
: APPLICATION NUMBER: US/09/908,322
: FILING DATE: 17-Jul-2001
: CLASSIFICATION: <unknown>
: PRIOR APPLICATION DATA:
: APPLICATION NUMBER: 08/981,392
: FILING DATE: 22-DEC-1997
: ATTORNEY/AGENT INFORMATION:
: NAME: Mistock, S Leslie
: REGISTRATION NUMBER: 18,872
: REFERENCE/DOCKET NUMBER: 7326-123
: TELECOMMUNICATION INFORMATION:

```

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TELEPHONE: 212-790-9090
TELEFAX: 212-869-8864
TELEX: 66141 PENNIE
INFORMATION FOR SEQ ID NO: 5:
SEQUENCE CHARACTERISTICS:
    LENGTH: 721 amino acids
    TYPE: amino acid
    STRANDEDNESS: <Unknown>
    TOPOLOGY: unknown
    MOLECULE TYPE: peptide
    SEQUENCE DESCRIPTION: SEQ ID NO: 5:
US-09-908-322-5

Query Match          55.0%; Score 66; DB 10; Length 721;
Best Local Similarity 32.0%; Pred. No. 24;
Matches      8; Conservative 11; Mismatches 6; Indels 0; Gaps 0;

QY      2 XIXMXCXKXLDCCSXKXNNXNC 26
      :  ::::|::|::|::|
Db      436 GFGSRNCDDNLDCTSFPCQNGTC 460

RESULT 4
US-09-894-882-168
: Sequence 168, Application US/09894882
: Patent No. US20020102607A1
: GENERAL INFORMATION:
  APPLICANT: University of Utah Research Foundation
  APPLICANT: Cognetix, Inc.
  APPLICANT: Walker, Craig S.
  APPLICANT: Shetty, Reshma
  APPLICANT: Jimenez, Eliste C.
  APPLICANT: McIntosh, J. Michael
  APPLICANT: Oliveira, Baldomero M.
  APPLICANT: Watkins, Maren
  APPLICANT: Jones, Robert M.
  APPLICANT: Shen, Greg S.
  TITLE OF INVENTION: I-Superfamily Conotoxins
  FILE REFERENCE: 2314-238
  CURRENT APPLICATION NUMBER: US/09/894,882
  PRIOR FILING DATE: 2001-06-29
  PRIOR APPLICATION NUMBER: US 60/
  PRIOR FILING DATE: 2000-06-30
  PRIOR APPLICATION NUMBER: US 60/243,410
  PRIOR FILING DATE: 2000-10-27
  PRIOR APPLICATION NUMBER: US 60/246,581
  PRIOR FILING DATE: 2000-11-08
  PRIOR APPLICATION NUMBER: US 60/247,714
  PRIOR FILING DATE: 2000-11-14
  PRIOR APPLICATION NUMBER: US 60/264,256
  PRIOR FILING DATE: 2001-01-29
  NUMBER OF SEQ ID NOS: 506
  SOFTWARE: PatentIn version 3.0
  SEQ ID NO 168
  LENGTH: 36
  TYPE: PRT
  ORGANISM: Conus betulinus
  FEATURE:
    NAME/KEY: PEPTIDE
    LOCATION: (1)..(36)
    OTHER INFORMATION: Xaa at residue 10 is Glu or gamma-carboxy-Glu; Xaa at residues
    OTHER INFORMATION: , 23 and 36 is Tyr, 125I-Tyr, mono-Iodo-Tyr, di-Iodo-Tyr, O-su
    OTHER INFORMATION: O-Tyr or O-phospho-Ty
US-09-894-882-168

Query Match          54.6%; Score 65.5; DB 10; Length 36;
Best Local Similarity 44.4%; Pred. No. 1.7;
Matches      12; Conservative 9; Mismatches 5; Indels 1; Gaps 1;

QY      1 CXIXNCKCXKXLDCCSXKXNNXNCV 27
      :  ::|::|::|::|::|::|::|
Db      2 CUSLGGQRCXRH-SDCCGXLCFCFXDKCV 27

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Page 3

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      PRIOR FILING DATE: 2000-11-14
      PRIOR APPLICATION NUMBER: US 60/264,256
      PRIOR FILING DATE: 2001-01-29
      NUMBER OF SEQ ID NOS: 506
      SOFTWARE: PatentIn version 3.0
      SEQ ID NO 167
      LENGTH: 73
      TYPE: PRT
      ORGANISM: Conus betulinus
US-09-894-882-167

Query Match          54.6%; Score 65.5; DB 10; Length 73;
Best Local Similarity 33.3%; Pred. No. 3.3;
Matches           9; Conservative 12; Mismatches        5; Indels     1; Gaps       1.

QY      1 CXIXNXXCXOXLDCCSXKXNNXKV 27
      |:|:::||||::||::||::||
DB      39 CLSLGRCERH-SDCGGLCCFYDKCV 64

RESULT 7
US-09-894-882-364
Sequence 364, Application US/09894882
Patent No. US20020102607A1
GENERAL INFORMATION:
APPLICANT: University of Utah Research Foundation
APPLICANT: Cognetix, Inc.
APPLICANT: Walker, Craig S.
APPLICANT: Shetty, Reshma
APPLICANT: Jimenez, Elsie C.
APPLICANT: McIntosh, J. Michael
APPLICANT: Olivera, Baldomero M.
APPLICANT: Watkins, Maren
APPLICANT: Jones, Robert M.
APPLICANT: Shen, Greg S.
TITLE OR INVENTION: I-Superfamily Conotoxins
FILE REFERENCE: 2314-238
CURRENT APPLICATION NUMBER: US/09/894,882
PRIOR FILING DATE: 2001-06-29
PRIOR APPLICATION NUMBER: US 60/
PRIOR FILING DATE: 2000-06-30
PRIOR APPLICATION NUMBER: US 60/243,410
PRIOR FILING DATE: 2000-10-27
PRIOR APPLICATION NUMBER: US 60/246,581
PRIOR FILING DATE: 2000-11-08
PRIOR APPLICATION NUMBER: US 60/247,714
PRIOR FILING DATE: 2000-11-14
PRIOR APPLICATION NUMBER: US 60/264,256
PRIOR FILING DATE: 2001-01-29
NUMBER OF SEQ ID NOS: 506
SOFTWARE: PatentIn version 3.0
SEQ ID NO 364
LENGTH: 32
TYPE: PRT
ORGANISM: Conus bruneus
US-09-894-882-364

Query Match          53.8%; Score 64.5; DB 10; Length 32;
Best local similarity 33.3%; Pred. No. 1.9;
Matches           9; Conservative 10; Mismatches        7; Indels     1; Gaps       1.

QY      1 CXIXNXGXOXLDCCSXKXNNXKV 27
      |:|:::||||::||::||::||
DB      1 CGYVGQDDDD-SDCGGLCCVAGECV 26

RESULT 8
US-09-894-882-413
Sequence 413, Application US/09894882
Patent No. US20020102607A1
GENERAL INFORMATION:
APPLICANT: University of Utah Research Foundation
APPLICANT: Cognetix, Inc.
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US-09-894-882-119
ORGANISM: Conus magus

Query Match
Best Local Similarity 53.8%; Score 64.5; DB 10; Length 71;
Matches 9; Conservative 11; Mismatches 6; Indels 1; Gaps 1;

CY      1 CXINMOXCXOXLDCCSXKCNMXNCV 27
       1:::1:::111:::1:::11
Db      39 CSLIQGRCSDH-SDCCMDMCCASEKY 64

RESULT 10
US-09-894-882-324
Sequence 324 Application US/09894882
Patent No. US20020102607A1
GENERAL INFORMATION:
APPLICANT: University of Utah Research Foundation
APPLICANT: Cognetix, Inc.
APPLICANT: Walker, Craig S.
APPLICANT: Shetty, Reshma J.
APPLICANT: Jimenez, Eslie C.
APPLICANT: McIntosh, J. Michael
APPLICANT: Oliveira, Baldomero M.
APPLICANT: Watkins, Maeha
APPLICANT: Jones, Robert M.
APPLICANT: Shen, Greg S.
TITLE OF INVENTION: 1-superfamily1 Coronoxins
FILE REFERENCE: 2314-238
CURRENT APPLICATION NUMBER: US/09/894,882
CURRENT FILING DATE: 2001-06-29
PRIOR APPLICATION NUMBER: US 60/
PRIOR FILING DATE: 2000-06-30
PRIOR APPLICATION NUMBER: US 60/243,410
PRIOR FILING DATE: 2000-10-27
PRIOR APPLICATION NUMBER: US 60/246,581
PRIOR FILING DATE: 2000-11-08
PRIOR APPLICATION NUMBER: US 60/247,714
PRIOR FILING DATE: 2000-11-14
PRIOR APPLICATION NUMBER: US 60/264,256
PRIOR FILING DATE: 2001-01-29
NUMBER OF SEQ ID NOS: 506
SOFTWARE: PatentIn version 3.0
SEQ ID NO: 324
LENGTH: 36
TYPE: PRT
ORGANISM: Conus episcopatius
FEATURE:
NAME/KEY: PEPTIDE
LOCATION: (1)..(36)
OTHER INFORMATION: Xaa at residue 36 is Pro or hydroxy-Pro; Xaa at residue 23 is
OTHER INFORMATION: , 125I-Tyr, mono-Iodo-Tyr, di-Iodo-Tyr, O-sulpho-Tyr or O-phos
US-09-894-882-324

Query Match
Best Local Similarity 52.9%; Score 63.5; DB 10; Length 36;
Matches 10; Conservative 9; Mismatches 6; Indels 1; Gaps 1;

QY      1 CXINMOXCXOXLDCCSXKCNMXNCV 26
       1:::1:::111:::1:::11
Db      3 CSRIQGCGGD-SDCCGMCCXQIC 27

RESULT 11
US-09-894-882-339
Sequence 339 Application US/09894882
Patent No. US20020102607A1
GENERAL INFORMATION:
APPLICANT: University of Utah Research Foundation
APPLICANT: Cognetix, Inc.
APPLICANT: Walker, Craig S.
APPLICANT: Shetty, Reshma

```

```
APPLICANT: Jimenez, Elsie C.
APPLICANT: McIntosh, J. Michael
APPLICANT: Olivera, Baldomero M.
APPLICANT: Watkins, Maren
APPLICANT: Jones, Robert M.
APPLICANT: Shen, Greg S.
TITLE OF INVENTION: I-Superfamily Conotoxins
FILE REFERENCE: 2314-238
CURRENT APPLICATION NUMBER: US/09/894,882
CURRENT FILING DATE: 2001-06-29
PRIOR APPLICATION NUMBER: US 60/
PRIOR FILING DATE: 2000-06-30
PRIOR APPLICATION NUMBER: US 60/243,410
PRIOR FILING DATE: 2000-10-27
PRIOR APPLICATION NUMBER: US 60/246,581
PRIOR FILING DATE: 2000-11-08
PRIOR APPLICATION NUMBER: US 60/247,714
PRIOR FILING DATE: 2000-11-14
PRIOR APPLICATION NUMBER: US 60/264,256
PRIOR FILING DATE: 2001-01-29
NUMBER OF SEQ ID NOS: 506
SOFTWARE: PatentIn version 3.0
SEQ ID NO 339
LENGTH: 36
TYPE: PRT
ORGANISM: Conus episcopus
FEATURE: PEPTIDE
NAME/KEY: (36)
LOCATION: (1)..(36)
OTHER INFORMATION: Xaa at residue 36 is Pro or hydroxy-Pro
US-09-894-882-339
```

```
Query Match          52.9%; Score 63.5; DB 10; Length 36;
Best Local Similarity 34.6%; Pred. No. 2.6;
Matches 9; Conservative 10; Mismatches 6; Indels 1; Gaps 1;
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```
QY 1 CXINQXQXLDCCSXKXNXXNC 26
| : | : | : | | : | : | : |
Db 3 CSRIQGGCGD-SDCCGDMCHGQIC 27
```

```
RESULT 12
US-09-894-882-441
Sequence 441, Application US/09894882
Patent No. US20020102607A1
GENERAL INFORMATION:
APPLICANT: University of Utah Research Foundation
APPLICANT: Cognetix, Inc.
APPLICANT: Walker, Craig S.
APPLICANT: Shetty, Reshma
APPLICANT: Jimenez, Elsie C.
APPLICANT: McIntosh, J. Michael
APPLICANT: Olivera, Baldomero M.
APPLICANT: Watkins, Maren
APPLICANT: Jones, Robert M.
APPLICANT: Shen, Greg S.
TITLE OF INVENTION: I-Superfamily Conotoxins
FILE REFERENCE: 2314-238
CURRENT APPLICATION NUMBER: US/09/894,882
CURRENT FILING DATE: 2001-06-29
PRIOR APPLICATION NUMBER: US 60/
PRIOR FILING DATE: 2000-06-30
PRIOR APPLICATION NUMBER: US 60/243,410
PRIOR FILING DATE: 2000-10-27
PRIOR APPLICATION NUMBER: US 60/246,581
PRIOR FILING DATE: 2000-11-08
PRIOR APPLICATION NUMBER: US 60/247,714
PRIOR FILING DATE: 2000-11-14
PRIOR APPLICATION NUMBER: US 60/264,256
PRIOR FILING DATE: 2001-01-29
NUMBER OF SEQ ID NOS: 506
SOFTWARE: PatentIn version 3.0
SEQ ID NO 441
```

```
LENGTH: 36
TYPE: PRT
ORGANISM: Conus episcopus
US-09-894-882-441
```

```
Query Match          52.9%; Score 63.5; DB 10; Length 36;
Best Local Similarity 34.6%; Pred. No. 2.6;
Matches 9; Conservative 10; Mismatches 6; Indels 1; Gaps 1;
```

```
QY 1 CXINQXQXLDCCSXKXNXXNC 26
| : | : | : | | : | : | : |
Db 3 CSRIQGGCGD-SDCCGDMCHGQIC 27
```

```
RESULT 13
US-09-894-882-443
Sequence 443, Application US/09894882
Patent No. US20020102607A1
GENERAL INFORMATION:
APPLICANT: University of Utah Research Foundation
APPLICANT: Cognetix, Inc.
APPLICANT: Walker, Craig S.
APPLICANT: Shetty, Reshma
APPLICANT: Jimenez, Elsie C.
APPLICANT: McIntosh, J. Michael
APPLICANT: Olivera, Baldomero M.
APPLICANT: Watkins, Maren
APPLICANT: Jones, Robert M.
APPLICANT: Shen, Greg S.
TITLE OF INVENTION: I-Superfamily Conotoxins
FILE REFERENCE: 2314-238
CURRENT APPLICATION NUMBER: US/09/894,882
CURRENT FILING DATE: 2001-06-29
PRIOR APPLICATION NUMBER: US 60/
PRIOR FILING DATE: 2000-06-30
PRIOR APPLICATION NUMBER: US 60/243,410
PRIOR FILING DATE: 2000-10-27
PRIOR APPLICATION NUMBER: US 60/246,581
PRIOR FILING DATE: 2000-11-08
PRIOR APPLICATION NUMBER: US 60/247,714
PRIOR FILING DATE: 2000-11-14
PRIOR APPLICATION NUMBER: US 60/264,256
PRIOR FILING DATE: 2001-01-29
NUMBER OF SEQ ID NOS: 506
SOFTWARE: PatentIn version 3.0
SEQ ID NO 443
LENGTH: 36
TYPE: PRT
ORGANISM: Conus episcopus
US-09-894-882-443
```

```
Query Match          52.9%; Score 63.5; DB 10; Length 36;
Best Local Similarity 34.6%; Pred. No. 2.6;
Matches 9; Conservative 10; Mismatches 6; Indels 1; Gaps 1;
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```
QY 1 CXINQXQXLDCCSXKXNXXNC 26
| : | : | : | | : | : | : |
Db 3 CSRIQGGCGD-SDCCGDMCHGQIC 27
```

```
RESULT 14
US-09-894-882-323
Sequence 323, Application US/09894882
Patent No. US20020102607A1
GENERAL INFORMATION:
APPLICANT: University of Utah Research Foundation
APPLICANT: Cognetix, Inc.
APPLICANT: Walker, Craig S.
APPLICANT: Shetty, Reshma
APPLICANT: Jimenez, Elsie C.
APPLICANT: McIntosh, J. Michael
APPLICANT: Olivera, Baldomero M.
APPLICANT: Watkins, Maren
```

```
QY      1 CXIXNQXCXQXLDDCCSXXCXNXXNC 26
        |: : |: |: | | :| :| :|
Db      39 CSRIGGCGGD-SDCCGDMCHGQIC 63
```

Query Match	52.98;	Score 63.5;	DB 10;	Length 72;
Best Local Similarity	34.68;	Pred. No. 4.9;		
Matches	9;	Conservative	10;	Mismatches 6;
				Indels 1;
				Gaps 1;

GenCore version 5.1.3  
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OM protein - protein search, using sw model

Run on: January 14, 2003, 18:29:51 ; Search time 16 Seconds  
(without alignments)  
162.227 Million cell updates/sec

Title: US-09-666-837B-1  
Perfect score: 120  
Sequence: 1 CXIXNQKXQXHLDDCCSXKXNKNXCV 27

Scoring table: BLOSUM62DX  
Gapop 10.0 , Gapext 0.5

Searched: 283224 seqs, 96134422 residues  
Total number of hits satisfying chosen parameters: 283224

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%

Listing first 45 summaries

Database :  
1: PIR-73:\*  
2: PIR1:\*  
3: PIR2:\*  
4: PIR3:\*  
5: PIR4:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	120	100.0	27	2	A58997 kappa-conotoxin PV
2	77	64.2	26	2	C44379 omega-conotoxin SV
3	72	60.0	2524	2	A35844 Notch protein - Af
4	69	57.5	29	2	UHO699 omega-conotoxin MV
5	68	56.7	2555	2	A40043 Notch protein homo
6	67	55.8	293	2	B26637 neurogenic repetit
7	67	55.8	2139	2	A35672 crumb protein - f
8	67	55.8	2437	2	S42612 transmembrane prot
9	67	55.8	2531	2	S18188 Notch protein homo
10	67	55.8	2531	2	A46019 Notch-1 protein -
11	66	55.0	29	2	B43620 omega-conotoxin GV
12	66	55.0	1203	2	A49175 Notch B protein -
13	66	55.0	2471	2	A49128 cell-fate determin
14	66	55.0	2703	1	A24420 Notch protein - fir
15	65	54.2	601	2	T22025 hypothetical prote
16	65	54.2	601	2	D89711 protein F40E10.4 l
17	65	54.2	1964	2	T09059 Notch4 - mouse
18	65	54.2	2318	2	S45306 Notch 3 protein -
19	65	54.2	2321	2	S78549 Notch3 protein - h
20	65	54.2	2531	2	T31070 Notch homolog - se
21	64	53.3	1372	2	T25933 Notch homolog prote
22	64	53.3	2352	2	T30201 Notch homolog prot
23	64	53.3	3623	2	T08618 Notch factor-B
24	63	52.5	43	2	S18174 metallothionein -
25	63	52.5	570	2	A48836 fibropellin C prec
26	63	52.5	1687	2	T30176 EGF repeat transme
27	62	51.7	29	2	A43620 omega-conotoxin GV
28	62	51.7	722	2	I48324 DELTA-like 1 - mou
29	62	51.7	1064	2	A40136 fibropellin Ia - s

30	61.5	51.2	36	1	A32038 mu-agatoxin I - fu
31	61	50.8	29	2	A58537 omega-conotoxin MV
32	61	50.8	728	2	C-Delta-1 - Chloke
33	61	50.8	1025	2	T42626 secreted leucine-r
34	61	50.8	1408	2	S16148 gene serrate prote
35	61	50.8	1469	2	B36655 slit protein 2 pre
36	61	50.8	1480	2	A36665 slit protein 1 pre
37	60	50.0	354	2	T22274 hypothetical prote
38	60	50.0	832	2	A31246 neurogenic protein
39	60	50.0	833	2	S19087 gene Delta protein
40	60	50.0	880	2	S00670 neurogenic repetit
41	60	50.0	1295	2	A32901 glp1 protein precu
42	60	50.0	1722	2	E89753 protein F1C7.4 li
43	59	49.2	25	2	JH0701 omega-conotoxin MV
44	59	49.2	43	2	S18173 metallothionein -
45	59	49.2	43	2	S33382 metallothionein -

## ALIGNMENTS

## RESULT 1

A58997 kappa-conotoxin PV1A - cone shell (Conus purpurascens)  
N:Alternate names: fin-popping peptide  
C:Species: Conus purpurascens (purple cone)  
C>Date: 23-Jul-1999 #sequence\_revision 23-Jul-1999 #text\_change 23-Jul-1999  
C:Accession: A58997  
R:Terlau, H.; Shon, K.J.; Grilley, M.; Stocker, M.; Stuehmer, W.; Olivera, B.M.  
Nature 381, 148-151, 1996  
A:Title: Strategy for rapid immobilization of prey by a fish-hunting marine snail.  
A:Reference number: A58997  
A:Accession: A58997  
A>Status: preliminary  
A:Molecule type: protein  
A:Residues: 1-27 <TRP>  
C:Comment: This conotoxin blocks conductance of the Shaker potassium channel.  
C:Keywords: hydroxyproline; neurotoxin; venom  
F:4/Modified site: 4-hydroxyproline (Pro) #status experimental

Query Match 100.0%; Score 120; DB 2; Length 27;  
Best Local Similarity 63.0%; Pred. No. 4.3e-05;  
Matches 17; Conservative 10; Mismatches 0; Indels 0; Gaps 0;

QY 1 CXIXNQKXQXHLDDCCSXKXNKNXCV 27  
DB 1 CRIPNQKCFHLDCCSRKCNREKVCV 27

## RESULT 2

C44379 omega-conotoxin SV1B [validated] - cone shell (Conus striatus)  
N:Alternate names: SNX-183  
C:Species: Conus striatus (striated cone)  
C>Date: 31-Dec-1993 #sequence\_revision 31-Dec-1993 #text\_change 15-Sep-2000  
C:Accession: C44379  
R:Ramilo, C.A.; Zafaralla, G.C.; Nadasdi, L.; Hammerland, L.G.; Yoshikami, D.; Gray, R.  
Biochemistry 31, 9919-9926, 1992  
A:Title: Novel alpha- and omega-conotoxins from Conus striatus venom.  
A:Reference number: A44379; MUID:93003172; PMID:1390774  
A:Accession: C44379  
A:Molecule type: protein  
A:Residues: 1-26 <RAM>  
A:Cross-references: CAS:143306-19-8  
A:Experimental source: venom  
A>Note: sequence extracted from NCBI backbone (NCBI:116002); structure confirmed by submitted to the Brookhaven Protein Data Bank, August 1996  
R:Nielsen, K.J.; Thomas, L.; Lewis, R.J.; Alewood, P.F.; Craik, D.J.  
A:Reference number: A67649; PDB:1MW7  
A:Contents: annotation; conformation by (1)H-NMR, residues 1-26  
J.Nielsen, K.J.; Thomas, L.; Lewis, R.J.; Alewood, P.F.; Craik, D.J.  
J. Mol. Biol. 263, 297-310, 1996  
A:Title: A consensus structure for omega-conotoxins with different selectivities for

A:Reference number: A58619; MUID:97070382; PMID:8913308  
A:Contents: annotation; conformation by (1)H-NMR  
C:Comment: This omega-conotoxin blocks presynaptic calcium channels.  
C:Superfamily: omega-conotoxin  
C:Keywords: acetylcholine release inhibition; amidated carboxyl end; calcium channel inh  
F:1-16,8-20,15-26/Disulfide bonds: #status predicted  
F:26/Modified site: amidated carboxyl end (Cys) #status experimental

Query Match 64.2%; Score 77; DB 2; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.42;  
Matches 9; Conservative 12; Mismatches 5; Indels 0; Gaps 0;

OY 1 CXIXNOXOXQXLDCCSXXCNXXNC 26  
DB 1 CKIKGSCRKISYDCSGSGCRGKC 26

RESULT 3  
A35844  
Xotch protein - African clawed frog  
C:Species: Xenopus laevis (African clawed frog)  
C:Date: 12-Oct-1990 #sequence\_revision 12-Oct-1990 #text\_change 02-Aug-2002  
C:Accession: A35844  
R:Coffman, C.; Harris, W.; Kintner, C.  
S:Science 249, 1438-1441, 1990  
A:Title: Xotch, the Xenopus homolog of Drosophila notch.  
A:Reference number: A35844; MUID:90385285; PMID:2402639  
A:Accession: A35844  
A:Status: preliminary; nucleic acid sequence not shown; not compared with conceptual tra  
A:Molecule type: mRNA  
A:Residues: 1-2524 <COE>  
C:Superfamily: notch protein; ankyrin repeat homology; EGF homology  
C:Keywords: transmembrane protein  
F:146-177/Domain: EGF homology <EGF1>  
F:184-215/Domain: EGF homology <EGF1>  
F:222-254/Domain: EGF homology <EGF3>  
F:456-487/Domain: EGF homology <EGF2>  
F:757-786/Domain: EGF homology <EGF3>  
F:1025-1056/Domain: EGF homology <EGF3>  
F:1924-1956/Domain: ankyrin repeat homology <AN1>  
F:1924-1956/Domain: ankyrin repeat homology <AN2>  
F:1957-1989/Domain: ankyrin repeat homology <AN2>  
F:1991-2023/Domain: ankyrin repeat homology <AN2>  
F:2024-2056/Domain: ankyrin repeat homology <AN2>  
F:2057-2089/Domain: ankyrin repeat homology <AN5>

Query Match 60.0%; Score 72; DB 2; Length 2524;  
Best Local Similarity 34.6%; Pred. No. 27;  
Matches 9; Conservative 12; Mismatches 5; Indels 0; Gaps 0;

OY 2 XIXNOXOXQXLDCCSXXCNXXNCV 27  
DB 248 GFGQNCENIDCPGNNCKNGACV 273

RESULT 4  
JH0699  
omega-conotoxin MVIC precursor [validated] - cone shell (Conus magus) (fragment)  
C:Species: Conus magus (magus cone)  
C:Date: 17-Apr-1993 #sequence\_revision 11-Apr-1997 #text\_change 15-Sep-2000  
C:Accession: JH0699; PC2380  
R:Hilliard, D.R.; Monje, V.D.; Mintz, I.M.; Bean, B.P.; Nadasdi, L.; Ramchandran, J.; M  
Neuron 9, 69-77, 1992  
A:Title: A new conus peptide ligand for mammalian presynaptic Ca2+ channels.  
A:Reference number: JH0699; MUID:92337922; PMID:1352986  
A:Accession: JH0699  
A:Molecule type: mRNA  
A:Residues: 1-29 <HIL>  
A:Cross-references: GB:S40826; NID:9252126; PIDN:AA82674.1; PID:9252127  
R:Nemoto, N.; Kubo, S.; Yoshida, T.; Chino, N.; Kimura, T.; Sakakibara, S.; Kyogoku, Y.;  
Biochem. Biophys. Res. Commun. 207, 695-700, 1995  
A:Title: Solution structure of omega-conotoxin MVIC determined by NMR.  
A:Reference number: PC2380; MUID:95169113; PMID:7864862  
A:Accession: PC2380

A:Molecule type: protein  
A:Residues: 3-28 <NEM>  
R:Farr-Jones, S.; Basus, V.J.  
submitted to the Brookhaven Protein Data Bank, December 1994  
A:Reference number: A66297; PDB:1OMN  
A:Contents: annotation; conformation by (1)H-NMR, residues 3-28  
R:Farr-Jones, S.; Miljanich, G.P.; Nadasdi, L.; Ramchandran, J.; Basus, V.J.  
J. Mol. Biol. 248, 106-124, 1995  
A:Title: Solution structure of omega-conotoxin MVIC, a high affinity of P-type calci  
A:Reference number: A58582; MUID:95248539; PMID:7731037  
A:Contents: annotation; conformation by (1)H-NMR  
C:Superfamily: omega-conotoxin  
C:Keywords: acetylcholine release inhibition; amidated carboxyl end; calcium channel  
F:3-28/Product: omega-conotoxin MVIC #status experimental <MAH>  
F:3-18,10-22,17-28/Disulfide bonds: #status experimental  
F:28/Modified site: amidated carboxyl end (Cys) (amide in mature form from following

Query Match 57.5%; Score 69; DB 2; Length 29;  
Best Local Similarity 30.8%; Pred. No. 2.5;  
Matches 8; Conservative 12; Mismatches 6; Indels 0; Gaps 0;

OY 1 CXIXNOXOXQXLDCCSXXCNXXNC 26  
DB 3 CKKGAPCRKRTMYDCSGSGCRGKC 28

RESULT 5  
A40043  
notch protein homolog TAN-1 precursor - human  
C:Species: Homo sapiens (man)  
C:Date: 21-Apr-1992 #sequence\_revision 21-Apr-1992 #text\_change 02-Aug-2002  
C:Accession: A40043  
R:Eilissen, L.W.; Bird, T.; West, D.C.; Soreng, A.L.; Reynolds, T.C.; Smith, S.D.; SK1  
Cell 66, 649-661, 1991  
A:Title: TAN-1, the human homolog of the Drosophila Notch gene, is broken by chromoso  
A:Reference number: A40043; MUID:91347367; PMID:1871692  
A:Accession: A40043  
A:Status: preliminary; nucleic acid sequence not shown; not compared with conceptual  
A:Molecule type: mRNA  
A:Residues: 1-2555 <EIL>  
A:Cross-references: GB:M73980  
C:Superfamily: notch protein; ankyrin repeat homology; EGF homology  
F:261-292/Domain: EGF homology <EGF1>  
F:494-525/Domain: EGF homology <EGF1>  
F:987-1018/Domain: EGF homology <EGF2>  
F:1149-1180/Domain: EGF homology <EGF2>  
F:1187-1218/Domain: EGF homology <EGF3>  
F:1233-1264/Domain: EGF homology <EGF3>  
F:1927-1959/Domain: ankyrin repeat homology <AN1>  
F:1960-1992/Domain: ankyrin repeat homology <AN2>  
F:1994-2026/Domain: ankyrin repeat homology <AN3>  
F:2027-2059/Domain: ankyrin repeat homology <AN3>  
F:2060-2092/Domain: ankyrin repeat homology <AN5>

Query Match 56.7%; Score 68; DB 2; Length 2555;  
Best Local Similarity 30.8%; Pred. No. 63;  
Matches 8; Conservative 12; Mismatches 6; Indels 0; Gaps 0;

OY 2 XIXNOXOXQXLDCCSXXCNXXNCV 27  
DB 248 GFTGQNCENIDCPGNNCKNGACV 273

RESULT 6  
B26637  
neurogenic repetitive locus 95F protein - fruit fly (Drosophila melanogaster) (fragme  
C:Species: Drosophila melanogaster  
C:Date: 16-Aug-1988 #sequence\_revision 16-Aug-1988 #text\_change 21-Jul-2000  
C:Accession: B26637  
R:Knust, E.; Dietrich, U.; Tepass, U.; Bremer, K.A.; Weigelt, D.; Vaessin, H.; Campos-  
EMBO J. 6, 761-766, 1987  
A:Title: EGF homologous sequences encoded in the genome of Drosophila melanogaster, a  
A:Reference number: A91081; MUID:87218537; PMID:3107986

```
A:Accession:326637
A:Molecule type:mRNA
A:Residues:1-293 <KNU>
A:Cross-references:GB:X05144; NID:g7519; PIDN:CAA28793.1; PID:g929536
C:Genetics:
A:Gene:FlyBase:crb
A:Cross-references:FlyBase:FBgn000368
C:Superfamily:unassigned EGF-related proteins; EGF homology
C:Keywords:transmembrane protein
F:139-170/Domain:EGF homology <EGx1>
F:177-208/Domain:EGF homology <EGf1>
F:216-252/Domain:EGF homology <EGF>

Query Match          55.8%; Score 67; DB 2; Length 293;
Best Local Similarity 28.0%; Pred.No. 18;
Matches      7; Conservative    13; Mismatches
                    5; Indels      0; Gaps      0.

QY      2 XIXNXCXOXLDCCSXNCXNNXXNC 26
       . : : | : : | : | : : | : : |
Db     164 GFEGHCEONIDECADQPCHNGNC 188
```

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RESULT 7
A:5672 crumbs protein - fruit fly (Drosophila melanogaster)
C:Species: Drosophila melanogaster
C>Date: 21-Sep-1990 #sequence_revision 18-Nov-1992 #text_change 11-Jan-2000
C:Accession: A35672
R:Tepass, U.; Theres, C.; Knust, E.
Cell 61, 787-799, 1990
Ar>Title: crumbs encodes an EGF-like protein expressed on apical membranes of Drosophila
Ar:Reference number: A35672; MUID:90263104; PMID:2344615
A:Accession: A35672
A>Status: preliminary
A:Molecule type: mRNA
A:Residues: 1-2139 <TRP>
Ar:Cross-references: GB:M3753
A>Note: the authors translated the codon GGC for residue 1928 as Cys, and TAT for residue
C:Genetics:
A:Gene: FLYBase:crb
Ar:Cross-references: FLYBase:FBgn0000368
C:Superfamily: unassigned EGF-related proteins; EGF homology
C:Keywords: Transmembrane protein
F:352-385/Domain: EGF homology <EGX1>
F:392-424/Domain: EGF homology <EGF1>
F:691-722/Domain: EGF homology <EGF>
F:767-799/Domain: EGF homology <EGF3>
F:1878-1914/Domain: EGF homology <EGX2>

Query Match          55.8%; Score 67; DB 2; Length 2139;
Best local Similarity 28.0%; Pred. No. 70;
Matches 7; Conservative 13; Mismatches 5; Indels 0; Gaps 0;

OY      2 XINQXCXQXLDDCCSXCNXXNXC 26
       :|::||::||:|::||:|
Db      1826 GFEGCHCEQNIDECADQPCHNGNC 1850

RESULT 8
S42612 transmembrane protein precursor - zebra fish
C:Species: Brachydanio rerio (zebra fish)
C>Date: 20-Feb-1995 #sequence_revision 20-Feb-1995 #text_change 02-Aug-2002
C:Accession: S42612
R:Bierkamp, C.; Campos-Ortega, J.A.
Mech. Dev. 43, 87-100, 1993
Ar>Title: A zebrafish homologue of the Drosophila neurogenic gene Notch and its pattern c
Ar:Reference number: S42612; MUID:94128602; PMID:8297791
A:Accession: S42612
A>Status: preliminary
A:Molecule type: mRNA
A:Residues: 1-2437 <BI>
Ar:Cross-references: EMBL:X69088; NID:g433866; PIDN:CAA48831.1; PID:g4433867

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C:Superfamily: notch protein; ankryrin repeat homology; EGF homology
F:735-766/Domain: EGF homology <EGF1>
F:1023-1054/Domain: EGF homology <EGF>
F:1185-1216/Domain: EGF homology <EGF2>
F:11915-1947/Domain: ankryrin repeat homology <AN1>
F:1948-1980/Domain: ankryrin repeat homology <AN2>
F:1982-2014/Domain: ankryrin repeat homology <AN3>
F:2015-2047/Domain: ankryrin repeat homology <AN4>
F:2048-2080/Domain: ankryrin repeat homology <AN5>

Query Match          55.8%; Score 67; DB 2; Length 2437;
Best Local Similarity 30.0%; Pred. No. 76;
Matches    9; Conservative   13; Mismatches      4; Indels     4; Gaps    1.
```

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RESULT 9
S18188
    notch protein homolog - rat
C:Species: Rattus norvegicus (Norway rat)
C:Date: 19-Feb-1994 #sequence_revision 10-Nov-1995 #text_change 02-Aug-2002
C:Accession: S18188
R:Weinmaster, G.; Roberts, V.J.; Lemke, G.
Development 113, 199-205, 1991
A:Title: A homolog of Drosophila Notch expressed during mammalian development.
A:Reference number: S18188; MUID:92111383; PMID:1764955
A:Accession: S18188
A:Molecule type: mRNA
A:Residues: 1-2531 <ME1>
A:Cross-references: EMBL:X57405; NID:957634; PID:957635
C:Superfamily: notch protein, ankyrin repeat homology; EGF homology
F:1025-1018/Domain: EGF homology <EGF1>
F:1025-1056/Domain: EGF homology <EGF>
F:1233-1264/Domain: EGF homology <EGF2>
F:1917-1949/Domain: ankyrin repeat homology <AN1>
F:1950-1982/Domain: ankyrin repeat homology <AN2>
F:1984-2016/Domain: ankyrin repeat homology <AN3>
F:2017-2049/Domain: ankyrin repeat homology <AN4>
F:2050-2082/Domain: ankyrin repeat homology <AN5>

Query Match          55.8%; Score 67; DB 2; Length 2531;
Best local Similarity 30.8%; Pred. NO. 78;
Matches 8; Conservative 12; Mismatches 6; Indels 0; Gaps 0;

QY      2 XIIXKXCXOXIDCCSXCNXXNCV 27
Db      248 GFAGQNCENVDPCGNCKNGACV 273
      ::|:::|||||::|::|::|

RESULT 10
A46019
Notch-1 protein - mouse
N:Alternate names: notch protein
C:Species: Mus musculus (house mouse)
C:Date: 22-Sep-1993 #sequence_revision 18-Nov-1994 #text_change 20-Sep-1999
C:Accession: A46019; S25144
R:del Amo, F.F.; Gendron-Maguire, M.; Swiatek, P.J.; Jenkins, N.A.; Copeland, N.G.; G
Genomics 15, 259-264, 1993
A:Title: Cloning, analysis, and chromosomal localization of Notch-1, a mouse homolog
A:Reference number: A46019; MUID:93194170; PMID:8449489
A:Accession: A46019
A:Status: not compared with conceptual translation
A:Molecule type: nucleic acid
A:Residues: 1-2531 <DE1>
A:Cross-references: GB:Z11886; GB:S47228; NID:9288502; PIDN:CA77941.1; PID:9288503
A:Note: sequence extracted from NCBI backbone (NCBI:127318)
R:Franco del Amo, F.; Smith, D.E.; Swiatek, P.J.; Gendron-Maguire, M.; Greenspan, R.J.
submitted to the EMBL Data Library, April 1992
A:Description: Expression pattern of Notch, a mouse homolog of Drosophila Notch, sugge
A:Reference number: S25144

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A:Accession: S25144  
A:Molecule type: mRNA  
A:Residues: 1551-2108, 'Q', 2110-2114, 'ALP', 2118-2170 <FRA>  
A:Cross-references: EMBL:Z11886  
C:Genetics:  
A:Gene: notch-1  
A:Map position: 2  
A>Note: proximal region of chromosome 2  
C:Superfamily: unassigned ankyrin repeat proteins; ankyrin repeat homology; EGF homology  
F:106-138/Domain: EGF homology <EGF1>  
F:144-175/Domain: EGF homology <EGF1>  
F:222-254/Domain: EGF homology <EGF2>  
F:261-292/Domain: EGF homology <EGF2>  
F:339-370/Domain: EGF homology <EGF3>  
F:416-449/Domain: EGF homology <EGF3>  
F:456-487/Domain: EGF homology <EGF4>  
F:494-525/Domain: EGF homology <EGF5>  
F:532-563/Domain: EGF homology <EGF6>  
F:607-638/Domain: EGF homology <EGF7>  
F:682-713/Domain: EGF homology <EGF8>  
F:757-788/Domain: EGF homology <EGF9>  
F:795-826/Domain: EGF homology <EGF10>  
F:873-904/Domain: EGF homology <EGF11>  
F:911-942/Domain: EGF homology <EGF12>  
F:949-980/Domain: EGF homology <EGF13>  
F:987-1018/Domain: EGF homology <EGF14>  
F:1025-1056/Domain: EGF homology <EGF15>  
F:1063-1094/Domain: EGF homology <EGF16>  
F:1149-1180/Domain: EGF homology <EGF17>  
F:1187-1218/Domain: EGF homology <EGF18>  
F:1233-1264/Domain: EGF homology <EGF19>  
F:1352-1383/Domain: EGF homology <EGF19>  
F:1391-1425/Domain: EGF homology <EGF>  
F:1917-1948/Domain: ankyrin repeat homology <AN1>  
F:1949-1981/Domain: ankyrin repeat homology <AN2>  
F:1983-2015/Domain: ankyrin repeat homology <AN3>  
F:2016-2048/Domain: ankyrin repeat homology <AN4>  
F:2049-2081/Domain: ankyrin repeat homology <AN5>  
  
Query Match 55.8%; Score 67; DB 2; Length 2531;  
Best Local Similarity 30.8%; Pred. No. 78;  
Matches 8; Conservative 12; Mismatches 6; Indels 0; Gaps 0;  
  
QY 2 XIXNXQXQXLDCCSXKXNXCXCV 27  
Db 248 GFAGQNCENVDPCGNCKNGACV 273  
  
RESULT 11  
B43620  
omega-conotoxin CVIIR - cone shell (Conus geographus)  
N:Alternate names: Shaker peptide GV11B  
C:Species: Conus geographus (geography cone)  
C>Date: 11-Dec-1992 #sequence\_revision 11-Dec-1992 #text\_change 23-May-1997  
C:Accession: B43620  
R:OLivera, B.M.; Gray, W.R.; Zeikus, R.; McIntosh, J.M.; Varga, J.; Rivier, J.; de Santis  
Science 230, 1338-1343, 1985  
A:Title: Peptide neurotoxins from fish-hunting cone snails.  
A:Reference number: A43620; MUID:86070213; PMID:4071055  
A:Accession: B43620  
A:Molecule type: protein  
A:Residues: 1-29 <OLI>  
C:Superfamily: omega-conotoxin  
C:Keywords: acetylcholine release inhibition; calcium channel inhibitor; hydroxyproline;  
F:1-16-8-19-15-26/disulfide bonds; #status predicted  
F:4,7/Modified site: 4-hydroxyproline (Pro) #status experimental  
  
Query Match 55.0%; Score 66; DB 2; Length 29;  
Best Local Similarity 26.9%; Pred. No. 4.8;  
Matches 7; Conservative 14; Mismatches 5; Indels 0; Gaps 0;  
  
QY 1 CXIXNXQXQXLDCCSXKXNXCXCV 26  
Db 1 CXIXNXQXQXLDCCSXKXNXCXCV 26

Db 1 CKSPGTCRGMRDCTCSLCSYKNC 26  
  
RESULT 12  
A49175  
Notch B protein - mouse (fragment)  
N:Alternate names: Notch homolog  
C:Species: Mus musculus (house mouse)  
C>Date: 21-Jan-1994 #sequence\_revision 05-Jan-1996 #text\_change 20-Sep-1999  
C:Accession: A49175; PMID:7570; S32113  
R:Cardelli, M.; Lendahl, U.  
Exp. Cell Res. 204, 364-372, 1993  
A:Title: Notch A and Notch B--two mouse Notch homologues coexpressed in a wide variety  
A:Reference number: A49175; MUID:93178563; PMID:8440332  
A:Accession: A49175  
A:Status: preliminary; nucleic acid sequence not shown  
A:Molecule type: mRNA  
A:Residues: 1-1203 <LAR>  
A:Cross-references: EMBL:X68279; NID:g287989; PIDN:CAA48340.1; PID:g287990  
A:Experimental source: embryo  
A>Note: sequence extracted from NCBI backbone (NCBI:P126158)  
C:Comment: This protein has many EGF repeats and 11n-12/Notch repeats.  
C:Superfamily: unassigned ankyrin repeat proteins; ankyrin repeat homology; EGF homol  
F:143-174/Domain: EGF homology <EGF1>  
F:148-513/Domain: EGF homology <EGF1>  
F:560-591/Domain: EGF homology <EGF>  
F:674-705/Domain: EGF homology <EGF2>  
F:712-743/Domain: EGF homology <EGF3>  
F:836-867/Domain: EGF homology <EGF3>  
  
Query Match 55.0%; Score 66; DB 2; Length 1203;  
Best Local Similarity 25.8%; Pred. No. 59;  
Matches 8; Conservative 14; Mismatches 5; Indels 4; Gaps 1;  
  
QY 1 CXIXN----QXQXQXLDCCSXKXNXCXCV 27  
Db 7 CVCVWMSGDCSENIDDCAVASCTPGSTCI 37  
  
RESULT 13  
A49128  
cell-fate determining gene Notch2 protein - rat  
C:Species: Rattus norvegicus (Norway rat)  
C>Date: 21-Jan-1994 #sequence\_revision 18-Nov-1994 #text\_change 02-Aug-2002  
C:Accession: A49128  
R:Weinmaster, G.; Roberts, V.J.; Lemke, G.  
Development 116, 931-941, 1992  
A:Title: Notch2: a second mammalian Notch gene.  
A:Reference number: A49128; MUID:93202015; PMID:1295745  
A:Accession: A49128  
A:Status: preliminary; not compared with conceptual translation  
A:Molecule type: mRNA  
A:Residues: 1-2471 <WEI>  
A:Experimental source: Schwann cell  
A>Note: sequence extracted from NCBI backbone (NCBI:P127811)  
C:Superfamily: notch protein; ankyrin repeat homology; EGF homology  
F:264-295/Domain: EGF homology <EGF1>  
F:799-830/Domain: EGF homology <EGF1>  
F:877-908/Domain: EGF homology <EGF2>  
F:1029-1060/Domain: EGF homology <EGF>  
F:1067-1098/Domain: EGF homology <EGF3>  
F:1153-1184/Domain: EGF homology <EGF3>  
F:1191-1222/Domain: EGF homology <EGF4>  
F:1876-1908/Domain: ankyrin repeat homology <AN1>  
F:1909-1941/Domain: ankyrin repeat homology <AN2>  
F:1943-1975/Domain: ankyrin repeat homology <AN3>  
F:1976-2008/Domain: ankyrin repeat homology <AN4>  
F:2009-2041/Domain: ankyrin repeat homology <AN5>  
  
Query Match 55.0%; Score 66; DB 2; Length 2471;  
Best Local Similarity 25.8%; Pred. No. 95;  
Matches 8; Conservative 14; Mismatches 5; Indels 4; Gaps 1;







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OM protein - protein search, using sw model

Run on: January 14, 2003, 18:29:11 ; Search time 11 Seconds  
(without alignments)  
101.806 Million cell updates/sec

Title: US-09-666-837B-1  
Perfect score: 120  
Sequence: 1 CXTXNQCKQXKXIDCCSXKXNKNXCV 27

Scoring table: BLOSUM62DX  
Gapop 10.0 , Gapext 0.5

Searched: 112892 seqs, 41476328 residues  
Total number of hits satisfying chosen parameters: 112892

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : SwissProt\_40:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	ID	Description
1	120	100.0	72	1	CKX7_CONPU
2	77	64.2	72	1	CKOB_CONST
3	73	60.8	26	1	CKOC_CONCT
4	72	60.0	2524	1	NOTC_XENIA
5	69	57.5	29	1	CKOC_CONMA
6	68	56.7	2556	1	NTC1_HUMAN
7	67	55.8	2139	1	CRB_DROME
8	67	55.8	2437	1	NTC1_BRABE
9	67	55.8	2531	1	NTC1_MOUSE
10	67	55.8	2531	1	NTC1_MOUSE
11	66	55.0	2470	1	NTC2_MOUSE
12	66	55.0	2471	1	NTC2_HUMAN
13	66	55.0	2471	1	NTC2_MOUSE
14	66	55.0	2703	1	NOTC_DROME
15	65	54.2	1964	1	NTC4_MOUSE
16	65	54.2	2319	1	NTC3_MOUSE
17	65	54.2	2321	1	NTC3_MOUSE
18	65	54.2	2321	1	NTC3_MOUSE
19	64	53.3	2003	1	NTC4_HUMAN
20	64	53.3	2003	1	NTC4_HUMAN
21	63	52.5	43	1	MTB_COLVT
22	63	52.5	570	1	FBP3_STRPU
23	63	52.5	589	1	DLI3_RAT
24	63	52.5	589	1	DLI3_RAT
25	63	52.5	589	1	DLI3_RAT
26	63	52.5	589	1	DLI3_RAT
27	63	52.5	589	1	DLI3_RAT
28	63	52.5	589	1	DLI3_RAT
29	63	52.5	589	1	DLI3_RAT
30	63	52.5	589	1	DLI3_RAT
31	63	52.5	589	1	DLI3_RAT
32	63	52.5	589	1	DLI3_RAT
33	63	52.5	589	1	DLI3_RAT

34	61.5	51.2	36	1	TXM1_AGEAP	P11057 agelenopsis
35	61	50.8	29	1	CKOD_CONMA	Q26350 conus magus
36	61	50.8	1408	1	SERR_DROME	P18168 drosophila
37	61	50.8	1480	1	SLIT_DROME	P24014 drosophila
38	60	50.0	833	1	DL_DROME	P10041 drosophila
39	60	50.0	1293	1	GLP1_CAEEL	P13508 caenorhabdit
40	60	50.0	1376	1	CRBH_HUMAN	P82279 homo sapien
41	59	49.2	25	1	CKOB_CONMA	P05485 conus magus
42	59	49.2	43	1	MTA_COLVT	P27086 colinus vir
43	59	49.2	53	1	CTL_NPVOP	O10367 oryza pseu
44	59	49.2	53	1	CTL_NPVAC	P41416 autographa
45	59	49.2	63	1	MT_CHICK	P09576 gallus gall

## ALIGNMENTS

RESULT 1  
ID CKX7\_CONPU STANDARD: PRT: 72 AA.  
AC P56633;  
DT 15-DEC-1998 (Rel. 37, Created)  
DT 15-JUN-2002 (Rel. 41, Last sequence update)  
DT 15-JUN-2002 (Rel. 41, Last annotation update)  
IDE Kappa-conotoxin PVIIA precursor (Fin-popping peptide).  
OS Conus purpurascens (Purple cone).  
OC Eukaryota; Metazoa; Mollusca; Gastropoda; Caenogastropoda;  
OC Neogastropoda; Conidae; Conus.  
OX NCBI\_TaxID=41690;  
RN [1]  
RN SEQUENCE FROM N.A., AND SYNTHESIS.  
RX MEDLINE=98079023; PubMed=9417043;  
RA Shon K.-J., Stocker M., Terlau H., Stuehmer W., Jacobsen R.B.,  
RA Walker C.S., Grille M.M., Watkins M., Hillyard D.R., Gray W.R.,  
RA Olivera B.M.;  
RT "Kappa-conotoxin PVIIA is a peptide inhibiting the shaker K+  
RT channel.";  
RL J. Biol. Chem. 273:33-38(1998).  
RN [2]  
RN SEQUENCE OF 46-72, AND SYNTHESIS.  
RX PubMed=12074021;  
RA Terlau H., Shon K.-J., Grille M.M., Stocker M., Stuehmer W.,  
RA Olivera B.M.;  
RT "Strategy for rapid immobilization of prey by a fish-hunting marine  
RT snail.";  
RL Nature 381:148-151(1996).  
RN [3]  
RN STRUCTURE BY NMR.  
RX TISSUE=Venom;  
RX MEDLINE=98104087; PubMed=9438859;  
RA Scanlon M.J., Naranjo D., Thomas L., Alewood P.F., Lewis R.J.,  
RA Craik D.J.;  
RT "Solution structure and proposed binding mechanism of a novel  
RT potassium channel toxin kappa-conotoxin PVIIA.";  
RL Structure 5:1585-1597(1997).  
RN [4]  
RN STRUCTURE BY NMR.  
RX MEDLINE=98217295; PubMed=9548922;  
RA Savarin P., Guenneugues M., Gilquin B., Lamthanh H., Gasparini S.,  
RA Zinn-Justin S., Menezes A.;  
RT "Three-dimensional structure of kappa-conotoxin PVIIA, a novel  
RT potassium channel-blocking toxin from cone snails.";  
RL Biochemistry 37:5407-5416(1998).  
RN [5]  
RN MUTAGENESIS OF ARG-47, ILE-48, PRO-49, ASN-50, GLN-51, LYS-52, PHE-54;  
RX PHE-54; GLN-55; HIS-56; LEU-57; ASP-58; SER-59; ARG-63;  
RX LYS-64; ARG-67; PHE-68; ASN-69 AND LYS-70.  
RX PubMed=10818087;  
RA Jacobsen R.B., Koch E.D., Lange-Malecki B., Stocker M., Verhey J.,  
RA Van Wagoner R.M., Vyzovkina A., Olivera B.M., Terlau H.;  
RT "Single amino acid substitutions in kappa-conotoxin PVIIA disrupt  
RT interaction with the shaker K+ channel.";  
RL J. Biol. Chem. 275:24639-24644(2000).

FT	DISULFID	46	61
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[illegible]

CC	Xenopodinae; Xenopus.
OX	NCBI_taxid=8355;
RN	[1]
RP	SEQUENCE FROM N.A.
RX	MEDLINE=90385285; PubMed=2402639;
RA	Coffman C., Harris W., Kintner C.;
RF	"Notch, the Xenopus homolog of Drosophila notch.";
RL	Science 249:1438-1441(1990).
RN	[2]
RP	REVISIONS TO 1759-1782.
RA	Kintner C.;
RL	Submitted (JUN-1996) to the EMBL/Genbank/DDBJ databases.
CC	-I- SUBCELLULAR LOCATION: Type I membrane protein.
CC	-I- DEVELOPMENTAL STAGE: EXPRESSED ALMOST UNIFORMLY IN EARLY EMBRYOS.
CC	-I- SIMILARITY: BELONGS TO THE NOTCH FAMILY.
CC	-I- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.
CC	-I- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.
CC	-I- SIMILARITY: CONTAINS 6 ANK REPEATS.
CC	-----
CC	This SWISS-PROT entry is copyright. It is produced through a collaboration
CC	between the Swiss Institute of Bioinformatics and the EMBL outstation
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CC	entities requires a license agreement (See <a href="http://www.isb-sib.ch/announce/or_send_an_email_to_license@sib-sib.ch">http://www.isb-sib.ch/announce/ or_send_an_email_to_license@sib-sib.ch</a> ).
CC	-----
DR	EMBL; M33874; AAB02039.1; -
DR	PIR; A35844; A35844.
DR	HSSP; P00740; 1EDM.
DR	InterPro; IPRO02110; ANK.
DR	InterPro; IPRO00152; Asx_hydroxyl.
DR	InterPro; IPRO00561; EGF-like.
DR	InterPro; IPRO00742; EGF_2.
DR	InterPro; IPRO01881; EGF_Ca.
DR	InterPro; IPRO01438; EGF_II.
DR	InterPro; IPRO00800; Notch.
DR	Pfam; PF00008; EGF; 36.
DR	Pfam; PF00023; ank; 6.
DR	Pfam; PF00066; notch; 3.
DR	PRINTS; PR00010; EGFBLOOD.
DR	PRINTS; PR01452; NOTCH.
DR	SMART; SM00248; ANK; 5.
DR	SMART; SM00179; EGF_CA; 23.
DR	SMART; SM00001; EGF_like; 11.
DR	SMART; SM00004; NL; 2.
DR	PROSITE; PS50088; ANK_REPEAT; 4.
DR	PROSITE; PS50297; ANK_REP_REGION; 1.
DR	PROSITE; PS00010; ASX_HYDROXYL; 23.
DR	PROSITE; PS00022; EGF_1; 34.
DR	PROSITE; PS01186; EGF_2; 29.
DR	PROSITE; PS01187; EGF_CA; 21.
KW	Differentiation; Neurogenesis; Repeat; ANK repeat; EGF-like domain; Transmembrane; Signal; Glycoprotein.
FT	SIGNAL 1 19 POTENTIAL.
FT	CHAIN 20 2524 NEUROGENIC LOCUS NOTCH PROTEIN HOMOLOG.
FT	DOMAIN 20 1728 EXTRACELLULAR (POTENTIAL).
FT	TRANSMEM 1729 1750 POTENTIAL.
FT	DOMAIN 1751 2524 CYTOPLASMIC (POTENTIAL).
FT	DOMAIN 20 57 EGF-LIKE 1.
FT	DOMAIN 58 99 EGF-LIKE 2.
FT	DOMAIN 102 140 EGF-LIKE 3.
FT	DOMAIN 141 177 EGF-LIKE 4.
FT	DOMAIN 179 215 EGF-LIKE 5.
FT	DOMAIN 217 254 EGF-LIKE 6.
FT	DOMAIN 256 292 EGF-LIKE 7.
FT	DOMAIN 294 332 EGF-LIKE 8.
FT	DOMAIN 334 370 EGF-LIKE 9.
FT	DOMAIN 371 409 EGF-LIKE 10.
FT	DOMAIN 411 449 EGF-LIKE 11.
FT	DOMAIN 451 487 EGF-LIKE 12.
FT	DOMAIN 489 525 EGF-LIKE 13.
FT	DOMAIN 527 563 EGF-LIKE 14.

FT	DOMAIN	565	600	EGF-LIKE 15,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	602	638	EGF-LIKE 16,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	640	673	EGF-LIKE 17,	EGF-LIKE 18,
FT	DOMAIN	677	713	EGF-LIKE 18,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	715	750	EGF-LIKE 19,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	752	788	EGF-LIKE 20,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	790	826	EGF-LIKE 21,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	828	866	EGF-LIKE 22,	EGF-LIKE 23,
FT	DOMAIN	868	904	EGF-LIKE 23,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	906	942	EGF-LIKE 24,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	944	980	EGF-LIKE 25,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	982	1018	EGF-LIKE 26,	EGF-LIKE 27,
FT	DOMAIN	1020	1056	EGF-LIKE 27,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	1058	1094	EGF-LIKE 28,	EGF-LIKE 29,
FT	DOMAIN	1096	1142	EGF-LIKE 29,	EGF-LIKE 30,
FT	DOMAIN	1144	1180	EGF-LIKE 30,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	1182	1218	EGF-LIKE 31,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	1220	1264	EGF-LIKE 32,	CALCIUM-BINDING (POTENTIAL).
FT	DOMAIN	1266	1304	EGF-LIKE 33,	EGF-LIKE 34,
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FT	DOMAIN	1347	1383	EGF-LIKE 35,	EGF-LIKE 36,
FT	DOMAIN	1386	1424	EGF-LIKE 36,	LIN/NOTCH 1.
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RL Neuron 9:69-77(1992).  
 RN [2]  
 RP STRUCTURE BY NMR.  
 RX MEDLINE-95248539; PubMed-7731037;  
 RA Farr-Jones S., Miljanich G.P., Nadasdi L., Ramachandran J.,  
 BA Basus V.J.;  
 RT "Solution structure of omega-conotoxin MV1IC, a high affinity ligand  
 of P-type calcium channels, using 1H NMR spectroscopy and complete  
 relaxation matrix analysis.";  
 RT J. Mol. Biol. 248:106-124(1995).  
 RL [3]  
 RP STRUCTURE BY NMR.  
 RX PubMed-10373375;  
 RA Nielsen K.J., Adams D., Thomas L., Bond T., Alewood P.F., Craik D.J.,  
 Lewis R.J.;  
 RT "Structure-activity relationships of omega-conotoxins MV1A, MV1IC and  
 RT 14 loop splice hybrids at N and P/Q-type calcium channels.";  
 RL J. Mol. Biol. 289:1405-1421(1999).  
 RN [4]  
 RP MUTAGENESIS OF TYR-15.  
 RX PubMed-7677735.  
 RA Kim J.I., Takahashi M., Martln-Moutot N., Seegar M.J., Ohtake A.,  
 Sato K.;  
 RT "Tyrl3 is essential for the binding of omega-conotoxin MV1IC to the  
 RT P/Q-type calcium channel.";  
 RL Biochem. Biophys. Res. Commun. 214:305-309(1995).  
 CC -1- FUNCTION: Omega-conotoxins act at presynaptic membranes, they bind  
 CC and block voltage-sensitive calcium channels (VSCC). This toxin  
 CC blocks N-type calcium channels as well as types of high-threshold  
 CC voltage-gated calcium channels resistant to both dihydropyridines  
 CC and omega-conotoxin GVIA.  
 CC -1- SUBCELLULAR LOCATION: Secreted.  
 CC -1- TISSUE SPECIFICITY: Expressed by the venom duct.  
 CC -1- SIMILARITY: BELONGS TO THE O-SUPERFAMILY OF CONOTOXINS. OMEGA-TYPE  
 CC FAMILY.  
 CC -----  
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 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
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 DR EMBL: S40826; JAB22674.1; -  
 DR PIR: JH0699; JH0699.  
 DR PDB: 1OMN; 01-DEC-95.  
 DR PDB: 1CNN; 31-MAY-00.  
 KW Presynaptic neurotoxin; Neurotoxin; Toxin; Calcium channel inhibitor;  
 KW Hydroxylation; Amidation; 3D-structure.  
 FT NON\_TER 1 1  
 FT PROPEP <1 2  
 FT BINDING 15 28 OMEGA-CONOTOXIN MV1IC.  
 FT DISULFID 3 18 ESSENTIAL FOR CALCIUM CHANNEL BINDING.  
 FT DISULFID 10 22  
 FT DISULFID 17 28  
 FT MOD\_RES 9 9 HYDROXYLATION (PROBABLE).  
 FT MOD\_RES 28 28 AMIDATION (G-29 PROVIDE AMIDE GROUP).  
 FT MUTAGEN 15 15 Y->A: HIGH DECREASE IN BINDING.  
 SQ SEQUENCE 29 AA: 3071 MW: ACTA68948474728A CRC64;  
 Query Match 57.5%; Score 69; DB 1; Length 29;  
 Best Local Similarity 30.8%; Pred. No. 0.35;  
 Matches 8; Conservative 12; Mismatches 6; Indels 0; Gaps 0;

ID NTCL\_HUMAN STANDARD; PRT; 2556 AA.  
 AC P46531;  
 DT 01-NOV-1995 (Rel. 32, Cited)  
 DT 15-JUN-2002 (Rel. 41, Last sequence update)  
 DT 15-JUN-2002 (Rel. 41, Last annotation update)  
 DE Neurogenic locus notch homolog protein 1 precursor (Notch 1) (hnl)  
 DE (Translocation-associated notch protein TAN-1).  
 GN NOTCH1 OR TAN1.  
 OS Homo sapiens (Human).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Primates; Catarrhini; Hominiidae; Homo.  
 OX NCBI\_TaxID=9606;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC Tissue-Brain;  
 RA Mann R.S., Blauweller C.M., Zagouras P.;  
 RT "Complete human notch 1 (hnl) cDNA sequence.";  
 RT Submitted (SEP-2000) to the EMBL/Genbank/DBJ databases.  
 RN [2]  
 RP SEQUENCE OF 1-2444 FROM N.A.  
 RX MEDLINE-91347367; PubMed-1831692;  
 RA Elisen L.W., Bird J., West D.C., Soreng A.L., Reynolds T.C.,  
 Smith S.D., Sklar J.;  
 RT "TAN-1, the human homolog of the Drosophila notch gene, is broken by  
 RT chromosomal translocations in T lymphoblastic neoplasms.";  
 RL Cell 66:649-661(1991).  
 RN [3]  
 RP IDENTIFICATION OF LIGANDS.  
 RX MEDLINE-99180765; PubMed-10079256;  
 RA Gray G.E., Mann R.S., Mitsiadis E., Henrique D., Carcangiu M.-L.,  
 Banks A., Leiman J., Ward D., Ish-Horowitz D., Artavanis-Tsakonas S.;  
 RT "Human ligands of the Notch receptor.";  
 RL Am. J. Pathol. 154:785-794(1999).  
 CC -1- FUNCTION: Functions as a receptor for membrane-bound ligands  
 CC jagged1, jagged2 and Delta1 to regulate cell-fate determination.  
 CC upon ligand activation through the released activator complex with  
 CC domain (NICD) it forms a transcriptional activator complex with  
 CC RBP-J/kappa and activates genes of the enhancer of split locus.  
 CC Affects the implementation of differentiation, proliferation and  
 CC apoptotic programs. May be important for normal lymphocyte  
 CC function. In altered form, may contribute to transformation or  
 CC progression in some T-cell neoplasms. Involved in the maturation  
 CC of both CD4+ and CD8+ cells in the thymus (By similarity).  
 CC -1- SUBUNIT: Heterodimer of a C-terminal fragment N(TW) and a N-  
 CC terminal fragment N(EC) which are probably linked by disulfide  
 CC bonds (By similarity).  
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein. Following  
 CC proteolytical processing NICD is translocated to the nucleus (By  
 CC similarity).  
 CC -1- TISSUE SPECIFICITY: In fetal tissues most abundant in spleen,  
 CC brain stem and lung. Also present in most adult tissues where it  
 CC is found mainly in lymphoid tissues.  
 CC -1- PTM: Synthesized in the endoplasmic reticulum as an inactive form  
 CC which is proteolytically cleaved by a furin-like convertase to yield  
 CC an active, ligand-accessible form. Cleavage results in a C-  
 CC terminal fragment N(TW) and a N-terminal fragment N(EC). Following  
 CC ligand binding, it is cleaved by TNF-alpha converting enzyme  
 CC (TACE) to yield a membrane-associated intermediate fragment called  
 CC notch extracellular truncation (NEXY). This fragment is then  
 CC cleaved by presenilin dependent gamma-secretase to release a  
 CC notch-derived peptide containing the intracellular domain (NICD)  
 CC from the membrane (By similarity).  
 CC -1- PTM: Phosphorylated (By similarity).  
 CC -1- DISEASE: Notch1 truncation is associated with neoplasia, a T-cell  
 CC acute lymphoblastic leukemia.  
 CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 CC -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
 CC -1- SIMILARITY: CONTAINS 5 ANK REPEATS.  
 CC -----  
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 DR EMBL: AF308602; AAC33848.1; -  
 DR EMBL: M73980; AAA60614.1; -  
 DR HSSP: P00740; IEDM.  
 DR Genew: HGNC:7881; NOTCH1.  
 DR MIM: 190198; -  
 DR InterPro: IPR002110; ANK.  
 DR InterPro: IPR000152; Asx\_hydroxyl.  
 DR InterPro: IPR000561; EGF-like.  
 DR InterPro: IPR00742; EGF\_2.  
 DR InterPro: IPR001881; EGF\_Ca.  
 DR InterPro: IPR001438; EGF\_11.  
 DR InterPro: IPR000800; Notch.  
 DR Pfam: PF00008; EGF; 36.  
 DR Pfam: PF00023; ank; 6.  
 DR Pfam: PF00066; notch; 3.  
 DR SMART: SM00246; ANK; 5.  
 DR SMART: SM00179; EGF\_Ca; 22.  
 DR SMART: SM00001; EGF\_like; 13.  
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 DR PROSITE: PS50297; ANK\_REPEAT\_REGION; 1.  
 DR PROSITE: PS00010; ASX\_HYDROXYL; 20.  
 DR PROSITE: PS00022; EGF\_1; 34.  
 DR PROSITE: PS01186; EGF\_2; 26.  
 DR PROSITE: PS01187; EGF\_Ca; 18.  
 DR Receptor: Transcription regulation; Activator; Differentiation;  
 KW Developmental protein; Repeat; ANK repeat; EGF-like domain;  
 KW Transmembrane; Glycoprotein; Signal; Phosphorylation.  
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 FT REPEAT 23980 24



OS Drosophila melanogaster (Fruit fly).  
 OC Eukaryota; Metazoa; Arthropoda; Mandibulata; Pancrustacea; Hexapoda;  
 OC Insecta; Pterygota; Neoptera; Endopterygota; Diptera; Brachycera;  
 OC Muscomorpha; Ephydroidea; Drosophilidae; Drosophila.  
 OX NCBI\_TaxID=7227;  
 RN (1)  
 RP SEQUENCE FROM N.A.  
 RC STRAIN-Oregon-R; TISSUE-Embryo;  
 RX MEDLINE=90263104; PubMed=2344615;  
 RA Tepas U., Theres C., Knust E.;  
 RT "Crumbs encodes an EGF-like protein expressed on apical membranes of  
 RT Drosophila epithelial cells and required for organization of  
 RT epithelia";  
 RL Cell 61:787-799(1990).  
 RN (2)  
 RP SEQUENCE OF 1663-1955 FROM N.A.  
 RC TISSUE-Embryo;  
 RX MEDLINE=87218537; PubMed=3107986;  
 RA Knust E., Dietrich U., Tepas U., Bremer K.A., Weigel D.,  
 RA Vaessin H., Campos-Ortega J.A.;  
 RT "EGF homologous sequences encoded in the genome of Drosophila  
 RT melanogaster, and their relation to neurogenic genes";  
 RL EMO J. 6:761-766(1987).  
 CC -1- FUNCTION: MAY PLAY A ROLE IN THE DEVELOPMENT OF EPITHELIA,  
 CC POSSIBLY FOR THE ESTABLISHMENT AND/OR MAINTENANCE OF CELL  
 CC POLARITY. IT MAY ACT AS A SIGNAL.  
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -1- PTM: PHOSPHORYLATED IN THE CYTOPLASMIC DOMAIN (POTENTIAL).  
 CC -1- SIMILARITY: CONTAINS 29 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 3 LAMININ G-LIKE DOMAINS.  
 CC -----  
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 CC -----  
 DR EMBL: M33753; AAA28428.1; ALT\_SEQ.  
 DR EMBL: X05144; CAA28793.1; -  
 DR PIR: B26637; B26637.  
 DR PIR: A35672; A35672.  
 DR HSP: P00740; IEDM.  
 DR FLYBase: FBgn0000368; crb.  
 DR InterPro: IPR000152; Asx\_hydroxyl.  
 DR InterPro: IPR000561; EGF-like.  
 DR InterPro: IPR000742; EGF\_2.  
 DR InterPro: IPR001881; EGF\_Ca.  
 DR InterPro: IPR001438; EGF\_II.  
 DR InterPro: IPR001791; Laminin\_G.  
 DR Pfam: PF00008; EGF\_26.  
 DR Pfam: PF00054; laminin\_G\_3.  
 DR PRINTS: PR00010; EGFRIOD.  
 DR SMART: SM00179; EGF\_CA; 11.  
 DR SMART: SM00001; EGF\_Like; 16.  
 DR SMART: SM00282; Lamg; 3.  
 DR PROSITE: PS00010; ASX\_HYDROXYL; 15.  
 DR PROSITE: PS00022; EGF\_1; 26.  
 DR PROSITE: PS01186; EGF\_2; 17.  
 DR PROSITE: PS01187; EGF\_CA; 12.  
 DR PROSITE: PS50025; LAM\_G\_DOMAIN; 3.  
 DR Differentiation: Repeat; EGF-like domain; Transmembrane;  
 KW Glycoprotein; Signal; Phosphorylation.  
 FT SIGNAL 1 90  
 FT CHAIN 91 2139 CRUMBS PROTEIN.  
 FT DOMAIN 91 2084 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 2085 2111 POTENTIAL.  
 FT DOMAIN 2112 2139 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 267 303 EGF-LIKE 1.  
 FT DOMAIN 306 343 EGF-LIKE 2.  
 FT DOMAIN 348 386 EGF-LIKE 3.  
 FT DOMAIN 388 425 EGF-LIKE 4, CALCIUM-BINDING (POTENTIAL).

FT DOMAIN 427 463 EGF-LIKE 5.  
 FT DOMAIN 464 500 EGF-LIKE 6.  
 FT DOMAIN 501 532 EGF-LIKE 7.  
 FT DOMAIN 545 581 EGF-LIKE 8.  
 FT DOMAIN 582 611 EGF-LIKE 9.  
 FT DOMAIN 609 646 EGF-LIKE 10.  
 FT DOMAIN 648 685 EGF-LIKE 11, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 687 723 EGF-LIKE 12, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 725 761 EGF-LIKE 13, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 763 800 EGF-LIKE 14, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 802 838 EGF-LIKE 15, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 840 902 EGF-LIKE 16.  
 FT DOMAIN 904 940 EGF-LIKE 17, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 942 978 EGF-LIKE 18, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 980 1021 EGF-LIKE 19.  
 FT DOMAIN 1023 1205 LAMININ G-LIKE 1.  
 FT DOMAIN 1207 1243 EGF-LIKE 20.  
 FT DOMAIN 1250 1480 LAMININ G-LIKE 2.  
 FT DOMAIN 1481 1517 EGF-LIKE 21.  
 FT DOMAIN 1558 1758 LAMININ G-LIKE 3.  
 FT DOMAIN 1759 1795 EGF-LIKE 22.  
 FT DOMAIN 1797 1833 EGF-LIKE 23, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 1835 1871 EGF-LIKE 24, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 1874 1915 EGF-LIKE 25.  
 FT DOMAIN 1915 1951 EGF-LIKE 26.  
 FT DOMAIN 1953 1989 EGF-LIKE 27, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 1991 2029 EGF-LIKE 28, CALCIUM-BINDING (POTENTIAL).  
 FT DOMAIN 2030 2070 EGF-LIKE 29.  
 FT DOMAIN 271 282 BY SIMILARITY.  
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 FT CARBOHYD 37 96 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 FT CARBOHYD 96 96 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 FT CARBOHYD 198 198 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 FT CARBOHYD 238 238 N-LINKED (GLCNAC. . .) (POTENTIAL).  
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 FT CARBOHYD 336 336 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 FT CARBOHYD 400 400 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 FT CARBOHYD 550 550 N-LINKED (GLCNAC. . .) (POTENTIAL).  
 Query Match 55.8%; Score 67; DB 1; Length 2139;  
 Best Local Similarity 28.0%; Pred. No 18;  
 Matches 7; Conservative 13; Mismatches 5; Indels 0; Gaps 0;

RC TISSUE=Embryo; PubMed=8297791;  
 RX MEDLINE=94128602; Campos-Ortega J.A.;  
 RA Bierkamp C.; "A zebrafish homolog of the Drosophila neurogenic gene Notch and  
 RT its pattern of transcription during early embryogenesis.";  
 RL Mech. Dev. 43:87-100(1993).  
 CC -1- FUNCTION: IMPLICATED IN CELL FATE SPECIFICATIONS DURING  
 CC EMBRYO DEVELOPMENT. MAY BE INVOLVED IN THE FORMATION OF THE  
 CC NEURAL PLATE, NOTOCHORD AND BRAIN VESICLES.  
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -1- DEVELOPMENTAL STAGE: Expressed in all cells in pregastrulation  
 CC stages. During gastrulation is differentially expressed,  
 CC accumulating predominantly in the prechordal mesoderm and  
 CC notochord. At the end of gastrulation, expressed along the  
 CC anterior-posterior axis including the developing neural plate  
 CC and differentiating mesoderm. Also present in the developing  
 CC brain and head regions.  
 CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 CC -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 6 ANK REPEATS.  
 CC -----  
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 CC -----  
 DR EMBL: X69088; CAA48831.1; -.  
 DR HSSP: P00740; IEDM.  
 DR ZFIN: ZDB-GENE-990415-173; notch1a.  
 DR InterPro: IPR002110; ANK.  
 DR InterPro: IPR000152; Asx\_hydroxyl.  
 DR InterPro: IPR000561; EGF\_Like.  
 DR InterPro: IPR000742; EGF\_2.  
 DR InterPro: IPR001881; EGF\_Ca.  
 DR InterPro: IPR001438; EGF\_II.  
 DR InterPro: IPR000800; Notch.  
 DR Pfam: PF00008; EGF; 36.  
 DR Pfam: PF00023; ank; 6.  
 DR Pfam: PF00066; notch; 3.  
 DR PRINTS: PR00010; EGFBLDOD.  
 DR PRINTS: PR01452; NOTCH.  
 DR SMART: SM00248; ANK; 5.  
 DR SMART: SM00179; EGF\_CA; 19.  
 DR SMART: SM00001; EGF\_Like; 16.  
 DR PROSITE: PS50089; ANK\_REPEAT; 4.  
 DR PROSITE: PS50297; ANK\_REPEAT\_REGION; 1.  
 DR PROSITE: PS00010; ASX\_HYDROXYL; 23.  
 DR PROSITE: PS00022; EGF\_1; 34.  
 DR PROSITE: PS01186; EGF\_2; 28.  
 DR PROSITE: PS01187; EGF\_CA; 22.  
 KW Receptor; Transcription regulation; Activator; Differentiation;  
 KW developmental protein; Neurogenesis; Repeat; ANK repeat;  
 KW EGF-like domain; Transmembrane; Glycoprotein; Signal.  
 FT SIGNAL 1 20 POTENTIAL.  
 FT CHAIN 21 2437 NEUROGENIC LOCUS NOTCH HOMOLOG PROTEIN 1.  
 FT DOMAIN 21 1724 EXTRACELLULAR (POTENTIAL).  
 FT TRANSMEM 1725 1747 POTENTIAL.  
 FT CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 1748 2437 CYTOPLASMIC (POTENTIAL).  
 FT DOMAIN 21 57 EGF-LIKE 1.  
 FT DOMAIN 58 98 EGF-LIKE 2.  
 FT DOMAIN 101 138 EGF-LIKE 3.  
 FT DOMAIN 139 175 EGF-LIKE 4.  
 FT DOMAIN 176 215 EGF-LIKE 5.  
 FT DOMAIN 217 254 EGF-LIKE 6.  
 FT DOMAIN 256 292 EGF-LIKE 7.  
 FT DOMAIN 294 332 EGF-LIKE 8.  
 FT DOMAIN 334 370 EGF-LIKE 9.  
 FT DOMAIN 371 409 EGF-LIKE 10.



[2] SEQUENCE OF 731-1899 FROM N.A. (ISOFORM 2), AND DEVELOPMENTAL STAGE.  
RP STRAIN-CD-1: TISSUE-Embryo;  
RX MEDLINE-93050801: Pubmed-1426644;  
RA Reaume A.G., Conlon R.A., Ziringibl R., Yamaguchi T.P., Rossant J.;  
RT "Expression analysis of a Notch homologue in the mouse embryo.";   
RL Dev. Biol. 154:377-387(1992).  
[3]  
RP SEQUENCE OF 1551-1647 FROM N.A. (ISOFORM 1), AND DEVELOPMENTAL STAGE.  
RC TISSUE-Embryo;  
RX MEDLINE-93048835: Pubmed-1425352;  
RA Franco del Amo F., Smith D.E., Swiatek P.J., Gendron-Maguire M.,  
RG Greenspan R.J., McMahon A.P., Gridley T.;  
RT "Expression pattern of Notch, a mouse homolog of Drosophila Notch,  
RT suggests an important role in early postimplantation mouse  
RT development.";   
RL Development 115:737-744(1992).  
[4]  
RP SEQUENCE OF 1161-1547 FROM N.A.  
RC STRAIN-C57BL/6 X CBA; TISSUE-Embryo;  
RX MEDLINE-93178563: Pubmed-8440332;  
RA Lardelli M., Lendahl U.;  
RT "Notch A and Notch B-two mouse Notch homologues coexpressed in a  
RT wide variety of tissues.";   
RL Exp. Cell Res. 204:364-372(1993).  
[5]  
RP SEQUENCE OF 1659-1673 FROM N.A.  
RX MEDLINE-99364499: Pubmed-10437788;  
RA Lee J.S., Ishimoto A., Yanagawa S.I.;  
RT "Murine leukemia provirus-mediated activation of the Notch1 gene leads  
RT to induction of HES-1 in a mouse T lymphoma cell line, DL-3.";   
RL FEBS Lett. 455:276-280(1999).  
[6]  
RP SEQUENCE OF 1950-2201 FROM N.A.  
RX MEDLINE-98029496: Pubmed-9384671;  
RA Messelrie M., Folio M., Nehls M., Eggert H., Boehm T.;  
RT "Dynamic changes in gene expression during in vitro differentiation of  
RT mouse embryonic stem cells.";   
RL Cytokines Cell. Mol. Ther. 1:139-143(1995).  
[7]  
RP SEQUENCE OF 1655-1659, CLEAVAGE BY FURIN-LIKE CONVERTASE, AND  
RP MUTAGENESIS OF 1651-ARG-GLN-ARG-ARG-1654.  
RX MEDLINE-98318619: Pubmed-9653148;  
RA Logeart F., Bessia C., Bron C., Lebail O., Jarrault S., Seidah N.G.,  
RT Israel A.;  
RT "The Notch1 receptor is cleaved constitutively by a furin-like  
RT convertase.";   
RL Proc. Natl. Acad. Sci. U.S.A. 95:8108-8112(1998).  
[8]  
RP PARTIAL SEQUENCE, AND POST-TRANSLATIONAL PROCESSING.  
RX MEDLINE-21523956: Pubmed-11518718;  
RA Saxena M.T., Schroeter E.H., Mumm J.S., Kopan R.;  
RT "Murine notch homologs (N1-4) undergo presenilin-dependent  
RT proteolysis.";   
RL J. Biol. Chem. 276:40268-40273(2001).  
[9]  
RP POST-TRANSLATIONAL PROCESSING.  
RX MEDLINE-21374376: Pubmed-1145941;  
RA Mizutani T., Taniguchi Y., Aoki T., Hashimoto N., Honjo T.;  
RT "Conservation of the biochemical mechanisms of signal transduction  
RT among mammalian Notch family members.";   
RL Proc. Natl. Acad. Sci. U.S.A. 98:9026-9031(2001).  
[10]  
RP FUNCTION: Functions as a receptor for membrane-bound ligands  
CC Jagged1, Jagged2 and Delta1 to regulate cell-fate determination.  
CC Upon ligand activation through the released notch intracellular  
CC domain (NICD) it forms a transcriptional activator complex with  
CC RBP-J kappa and activates genes of the enhancer of split locus.  
CC Affects the implementation of differentiation, proliferation and  
CC apoptotic programs (by similarity). May play an essential role in  
CC postimplantation development, probably in some aspect of cell  
CC specification and/or differentiation. May be involved in mesoderm  
CC development, somite formation and neurogenesis. Involved in the  
CC maturation of both CD4+ and CD8+ cells in the thymus.

CC -1 SUBUNIT: Heterodimer of a C-terminal fragment N(TM) and a N-  
CC terminal fragment N(EC) which are probably linked by disulfide  
CC bonds.  
CC -1 SUBCELLULAR LOCATION: Type I membrane protein. Following  
CC proteolytical processing NICD is translocated to the nucleus.  
CC -1 ALTERNATIVE PRODUCTS: 2 isoforms; 1 (shown here) and 2; may be  
CC produced by alternative splicing.  
CC -1 TISSUE SPECIFICITY: Highly expressed in the brain, lung and  
CC thymus. Expressed at lower levels in the spleen, bone-marrow,  
CC spinal cord, eyes, mammary gland, liver, intestine, skeletal  
CC muscle, kidney and heart.  
CC -1 DEVELOPMENTAL STAGE: First detected in the mesoderm at 7.5 d.p.c.  
CC By 8.5 d.p.c. highly expressed in presomitic mesoderm, mesenchyme  
CC and endothelial cells, while much lower levels are seen in the  
CC neuroepithelium. Between 9.5-10.5 d.p.c. expressed at high levels  
CC in the neuroepithelium. At 13.5 d.p.c. expressed in the surface  
CC ectoderm, eye and developing whisker follicles.  
CC -1 PTM: Synthesized in the endoplasmic reticulum as an inactive form  
CC which is proteolytically cleaved by a furin-like convertase in the  
CC trans-golgi network before it reaches the plasma membrane to yield  
CC an active, ligand-accessible form. Cleavage results in a C-  
CC terminal fragment N(TM) and a N-terminal fragment N(EC). Following  
CC ligand binding, it is cleaved by TNF-alpha converting enzyme  
CC (TACE) to yield a membrane-associated intermediate fragment called  
CC notch extracellular truncation (NEXT). This fragment is then  
CC cleaved by presenilin dependent gamma-secretase to release a  
CC notch-derived peptide containing the intracellular domain (NICD)  
CC from the membrane.  
CC -1 PTM: Phosphorylated.  
CC -1 SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
CC -1 SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
CC -1 SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
CC -1 SIMILARITY: CONTAINS 5 ANK REPEATS.  
CC -----  
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CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
CC -----  
DR EMBL: Z1886; CAA77941.1; -  
DR EMBL: L02613; AAK14898.1; -  
DR EMBL: X68278; CAA48339.1; -  
DR EMBL: AJ238029; CAA40733.1; -  
DR EMBL: X82562; CAA57909.1; -  
DR HSSP: P00740; 1EDM.  
DR MGD: MGI:97363; Notch1.  
DR InterPro: IPR002110; ANK.  
DR InterPro: IPR000152; Asx\_hydroxyl.  
DR InterPro: IPR000561; EGF-like.  
DR InterPro: IPR000742; EGF\_2.  
DR InterPro: IPR001881; EGF\_Ca.  
DR InterPro: IPR001438; EGF\_III.  
DR InterPro: IPR000800; Notch.  
DR Pfam: PF00008; EGF\_35.  
DR Pfam: PF00023; ank; 7.  
DR Pfam: PF00066; notch; 3.  
DR PRINTS: PR00010; EGFLOOD.  
DR PRINTS: PR01452; NOTCH.  
DR SMART: SM00248; ANK; 3.  
DR SMART: SM00179; EGF\_CA; 23.  
DR SMART: SM00001; EGF\_III; 11.  
DR SMART: SM00004; NL; 2.  
DR PROSITE: PS50068; ANK\_REPEAT; 2.  
DR PROSITE: PS50297; ANK\_REPEAT\_REGION; 1.  
DR PROSITE: PS00010; ASX\_HYDROXYL; 22.  
DR PROSITE: PS00022; EGF\_1; 34.  
DR PROSITE: PS01186; EGF\_2; 27.  
DR PROSITE: PS01187; EGF\_CA; 21.  
DR Receptor; Transcription regulation: Activator; Differentiation;  
DR Developmental protein: Repeat; ANK repeat; EGF-like domain;  
KW

"Notch1 and Notch3 instructively restrict bDNF-responsive multipotent neural progenitor cells to an astroglial fate.",  
RL Neuron 29:45-55(2001).  
[4]  
RP TISSUE SPECIFICITY.  
RX MEDLINE=93202015; PubMed=1295745;  
RA Weimaster G., Roberts V.J., Lemke G.;  
RT "Notch2: a second mammalian Notch gene."  
RN Development 116:931-941(1992).  
[5]  
RP TISSUE SPECIFICITY.  
RX MEDLINE=21311789; PubMed=11438922;  
RA Irvan D.K., Zurcher S.D., Nguyen T., Weimaster G., Kornblum H.I.;  
RT "Expression patterns of Notch1, Notch2, and Notch3 suggest multiple functional roles for the Notch-Delta signaling system during brain development."  
RL J. Comp. Neurol. 436:167-181(2001).  
I.- FUNCTION: Functions as a receptor for membrane-bound ligands jagged1, jagged2 and Delta1 to regulate cell-fate determination. Upon ligand activation through the released notch intracellular domain (NICD) it forms a transcriptional activator complex with RBP-J kappa and activates genes of the enhancer of split locus. Affects the implementation of differentiation, proliferation and apoptotic programs (By similarity). Acts instructively to control the cell fate determination of CNS multipotent progenitor cells, resulting in astroglial induction and neuron/oligodendrocyte suppression.  
I.- SUBUNIT: Heterodimer of a C-terminal fragment N(TM) and a N-terminal fragment N(EC) which are probably linked by disulfide bonds (By similarity).  
I.- SUBCELLULAR LOCATION: Type I membrane protein. Following proteolytical processing NICD is translocated to the nucleus (By similarity).  
I.- TISSUE SPECIFICITY: Expressed in the brain, kidney and spleen. Expressed in postnatal central nervous system (CNS) germinal zones and in early postnatal life, within numerous cells throughout the CNS. Found in both subventricular and ventricular germinal zones.  
I.- DEVELOPMENTAL STAGE: In the embryo, highest levels occur between days 12 and 14 and decrease rapidly to much lower levels in the adult.  
I.- PTM: Synthesized in the endoplasmic reticulum as an inactive form which is proteolytically cleaved by a furin-like convertase in the trans-Golgi network before it reaches the plasma membrane to yield an active, ligand-accessible form. Cleavage results in a C-terminal fragment N(TM) and a N-terminal fragment N(EC). Following ligand binding, it is cleaved by TNF-alpha converting enzyme (TACE) to yield a membrane-associated intermediate fragment called notch extracellular truncation (NEX). This fragment is then cleaved by presenilin dependent gamma-secretase to release a notch-derived peptide containing the intracellular domain (NICD) from the membrane (By similarity).  
I.- PTM: Phosphorylated (By similarity).  
I.- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
I.- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
I.- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
I.- SIMILARITY: CONTAINS 5 ANK REPEATS  
-----  
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CC -----  
DR EMBL; X57405; CAAt0667.1; -.  
DR HSSP; P00740; IEEM.  
DR InterPro; IPRO02110; ANK.  
DR InterPro; IPRO00152; ANK\_hydroxyl.  
DR InterPro; IPRO00561; EGF-like.  
DR InterPro; IPRO00742; EGF\_2.  
DR InterPro; IPRO01881; EGF-Ca.  
DR

DR InterPro: IPR002049; Lamln1\_EGF.  
 DR InterPro: IPR000800; Notch.  
 DR Pfam: PF00008; EGF\_36.  
 DR Pfam: PF00023; ank; 6.  
 DR Pfam: PF00066; notch; 3.  
 DR PRINTS: PR00010; EGFLOOD.  
 DR PRINTS: PR00011; EGFAMININ.  
 DR PRINTS: PR01452; NOTCH.  
 DR SMART: SM00248; ANK; 5.  
 DR SMART: SM00179; EGF\_CA; 25.  
 DR SMART: SM00001; EGF\_Like; 10.  
 DR SMART: SM00004; NL; 2.  
 DR PROSITE: PSS0088; ANK\_REPEAT; 4.  
 DR PROSITE: PSS0297; ANK\_REPEAT\_REGION; 1.  
 DR PROSITE: PSS0010; ASK\_HYDROXYL; 22.  
 DR PROSITE: PSS0022; EGF\_1; 35.  
 DR PROSITE: PSS0186; EGF\_2; 26.  
 DR PROSITE: PSS0187; EGF\_CA; 21.  
 KW Receptor; Transcription regulation; Activator; Differentiation;  
 KW Developmental protein; Repeat; ANK repeat; EGF-like domain;  
 KW Transmembrane; Glycoprotein; Signal; Phosphorylation.  
 FT SIGNAL 1 18  
 FT CHAIN 19 2531  
 FT CHAIN 1711 2531  
 FT CHAIN 1744 2531  
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 FT DOMAIN 641 676  
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 FT DOMAIN 1441 1480  
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 FT REPEAT 1523 1562  
 FT REPEAT 1517 1946  
 FT REPEAT 1950 1980  
 FT REPEAT 1984 2013  
 FT REPEAT 2017 2046

FT REPEAT 2050 2079 ANK 5.  
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 FT DOMAIN 1891 1894 POLY-GLU.  
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 FT DOMAIN 2497 2500 POLY-SER.  
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 Matches 8; Conservative 12; Mismatches 6; Indels 0; Gaps 0;  
 Oy 2 XIXNXXCXOXLDPCSSXXNXXNXXCV 27  
 DB 248 GPAGNCCENVDPCGNNCKNGACV 273  
 ID NTC2\_MOUSE STANDARD; PRT; 2470 AA.  
 AC 035516; 060941; 006008;  
 DT 15-JUN-2002 (Rel. 41, Created)  
 DT 15-JUN-2002 (Rel. 41, Last sequence update)  
 DE Neuregulin locus notch homolog protein 2 precursor (Notch 2) (Molch B).  
 DE GN NOTCH2.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathu; Muridae; Mus.  
 OX NCBI\_TaxID=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN=C57BL/6; TISSUE=Thymus;  
 RA Hanada Y., Higuchi M., Tsujimoto Y.;  
 RT "Complete amino acid sequence and mut11form transcripts encoded by a  
 RT single copy of mouse Notch2 gene.";  
 RL Submitted (JUL-1994) to the EMBL/GenBank/DBJ databases.  
 RN [2]  
 RP SEQUENCE OF 316-1518 FROM N.A.  
 RC STRAIN=C57BL/6 X CBA; TISSUE=Embryo;  
 RX MEDLINE=93178563; PubMed=8440332;  
 RA Lardelli M., Lendahl U.;  
 RT "Notch A and Notch B-two mouse Notch homologues coexpressed in a  
 RT wide variety of tissues.";  
 RL Exp. Cell Res. 204:364-372(1993).  
 RN [3]  
 RP SEQUENCE OF 1765-2153 FROM N.A.  
 RX MEDLINE=97075110; PubMed=8917536;  
 RA Milner L.A., Bigas A., Kopan R., Brashem-Stein C., Bernstein I.D.,  
 RA Martin D.I.;  
 RT "Inhibition of granulocytic differentiation by mNotch1.";  
 RT Proc. Natl. Acad. Sci. U.S.A. 93:13014-13019(1996).  
 RN [4]

RP FUNCTION: MEDLINE=99396706; PubMed=10393120;  
 RX Hamada Y., Kadokawa Y., Okabe M., Ikawa M., Coleman J. R.,  
 RA Tsujimoto Y.,  
 RT "Mutation in ankyrin repeats of the mouse Notch2 gene induces early  
 RT embryonic lethality".  
 RL development 126:3415-3424(1999).  
 RP DEVELOPMENTAL STAGE, AND ALTERNATIVE SPLICING.  
 RX MEDLINE=95333893; PubMed=7609614;  
 RA Higuchi M., Kiyama H., Hayakawa T., Hamada Y., Tsujimoto Y.,  
 RT "Differential expression of Notch1 and Notch2 in developing and adult  
 RT mouse brain".  
 RL Brain Res. Mol. Brain Res. 29:263-272(1995).  
 RP POST-TRANSLATIONAL PROCESSING, AND MUTAGENESIS OF MET-1699.  
 RX MEDLINE=21523956; PubMed=11518718;  
 RA Saxena M.T., Schroeter E.H., Mumm J.S., Kopan R.,  
 RT "Murine notch homologs (NL-4) undergo presenilin-dependent  
 RT proteolysis".  
 RL J. Biol. Chem. 276:40268-40273(2001).  
 RP POST-TRANSLATIONAL PROCESSING, AND MUTAGENESIS OF MET-1699.  
 RX MEDLINE=21374376; PubMed=11459941;  
 RA Mizutani T., Taniguchi Y., Aoki T., Hashimoto N., Honjo T.,  
 RT "Conservation of the biochemical mechanisms of signal transduction  
 RT among mammalian Notch family members".  
 RL Proc. Natl. Acad. Sci. U.S.A. 98:9026-9031(2001).  
 RP FUNCTION: Functions as a receptor for membrane-bound ligands  
 CC jagged, jagged2 and deltal to regulate cell-fate determination.  
 CC Upon ligand activation through the released notch intracellular  
 CC domain (NICD) it forms a transcriptional activator complex with  
 CC RBP-1 kappa and activates genes of the enhancer of split locus.  
 CC Affects the implementation of differentiation, proliferation and  
 CC apoptotic programs (By similarity). May play an essential role in  
 CC postimplantation development, probably in some aspect of cell  
 CC specification and/or differentiation.  
 CC SUBUNIT: Heterodimer of a C-terminal fragment N(TM) and a N-  
 CC terminal fragment N(EC) which are probably linked by disulfide  
 CC bonds.  
 RP SUBCELLULAR LOCATION: Type I membrane protein. Following  
 CC proteolytical processing NICD is translocated to the nucleus.  
 CC ALTERNATIVE PRODUCTS: 2 isoforms; 1 (shown here) and 2; may be  
 CC produced by alternative splicing.  
 CC TISSUE SPECIFICITY: Expressed in the brain, liver, kidney,  
 CC neuroepithelia, somites, optic vesicles and branchial arches, but  
 CC not heart.  
 RP DEVELOPMENTAL STAGE: Expressed in the embryonic ventricular zone,  
 CC the postnatal ependymal cells, and the choroid plexus throughout  
 CC embryonic and postnatal development.  
 RP PTM: Synthesized in the endoplasmic reticulum as an inactive form  
 CC which is proteolytically cleaved by a furin-like convertase in the  
 CC trans-Golgi network before it reaches the plasma membrane to yield  
 CC an active, ligand-accessible form. Cleavage results in a C-  
 CC terminal fragment N(TM) and a N-terminal fragment N(EC). Following  
 CC ligand binding, it is cleaved by TNF-alpha converting enzyme  
 CC (TACE) to yield a membrane-associated intermediate fragment called  
 CC notch extracellular truncation (NEXT). This fragment is then  
 CC cleaved by presenilin dependent gamma-secretase to release a  
 CC notch-derived peptide containing the intracellular domain (NICD)  
 CC from the membrane.  
 RP PTM: Phosphorylated.  
 RP SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 RP SIMILARITY: CONTAINS 34.5 EGF-LIKE DOMAINS.  
 RP SIMILARITY: CONTAINS 2 LIN/NOTCH REPEATS.  
 RP SIMILARITY: CONTAINS 6 ANK REPEATS.  
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[illegible]





[illegible]



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 Best Local Similarity 25.8%; Pred. No. 25;  
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 AC P07207; P04154; 097458; 09W4T8;  
 DT 01-NOV-1986 (Rel. 03, Created)  
 DT 15-JUN-2002 (Rel. 41, Last sequence update)  
 DT 15-JUN-2002 (Rel. 41, Last annotation update)  
 DE Neurogenic locus Notch protein precursor  
 GN N OR EG:140611.1 OR EG:163A10.2 OR CG3936.  
 OS Drosophila melanogaster (Fruit fly).  
 OC Eukaryota; Metazoa; Arthropoda; Mandibulata; Pancrustacea; Hexapoda;  
 OC Insecta; Pterygota; Neoptera; Endopterygota; Diptera; Brachycera;  
 OC Muscomorpha; Ephydroidea; Drosophilidae; Drosophila.  
 OC NCBI\_TaxID=7227;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN-Oregon-R; TISSUE-Embryo;  
 RX MEDLINE=86079539; PubMed=3935325;  
 RA Wharton K.A., Johansen K.M., Xu T., Artavanis-Tsakonas S.;  
 RT "Nucleotide sequence from the neurogenic locus notch implies a gene  
 RT product that shares homology with proteins containing EGF-like  
 RT repeats.";  
 RL Cell 43:567-581(1985).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN-Canton-S, and Oregon-R; TISSUE-Embryo;  
 RX MEDLINE=87064624; PubMed=3097517;  
 RA Kidd S., Kelley M.R., Young M.W.;  
 RT "Sequence of the notch locus of Drosophila melanogaster: relationship  
 RT of the encoded protein to mammalian clotting and growth factors.";  
 RL Mol. Cell. Biol. 6:3094-3108(1986).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN-Berkeley;  
 RX MEDLINE=20196006; PubMed=10731132;  
 RA Adams M.D., Celniker S.E., Holt R.A., Evans C.A., Gocayne J.D.,  
 RA Amanatides P.G., Scherer S.E., Li P.W., Hoskins R.A., Galle R.F.,  
 RA George R.A., Lewis S.E., Richards S., Ashburner M., Henderson S.N.,  
 RA Sutton G.G., Mortan J.R., Yandell M.D., Zhang Q., Chen L.X.,  
 RA Brandon R.C., Rogers Y.H.C., Blazej R.G., Champe M., Pfeiffer B.D.,  
 RA Wan K.H., Doyle C., Baxter E.G., Helt J., Nelson C.R., Milos G.L.G.,  
 RA Abril J.F., Aghayani A., An H.-J., Andrews-Pfannkoch C., Baldwin D.,  
 RA Ballew R.M., Basu A., Baxendale A., Bayraktaroglu L., Beasley E.M.,  
 RA Beeson K.Y., Benos P.V., Berman B.P., Bhandari D., Bolshakov S.,  
 RA Borokova D., Botchan M.R., Bouck J., Brokstein D., Brotlier P.,  
 RA Burks K.C., Busam D.A., Butler H., Cadieu E., Center A., Chandra I.,  
 RA Cherry J.M., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,  
 RA de Pablos B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,  
 RA Dodson K.J., Doup L.E., Downes M., Dugan-Rocha S., Dunkov B.C., Dunn P.,  
 RA Durbin K.J., Evangelista C.C., Ferraz C., Ferreira S., Fleischmann W.,  
 RA Fiesel G., Gabrielian A.E., Garg N.S., Gelbart W.M., Glasser K.,  
 RA Glodok A., Gong F., Gorrell J.H., Gu Z., Guan P., Harris M.,  
 RA Harris N.L., Harvey D., Heiman T.J., Hernandez J.R., Houck J.,  
 RA Hostin D., Houston K.A., Howland T.J., Wei M.-H., Idegvam C.,  
 RA Jalali M., Kalush F., Karpen G.H., Ke Z., Kennison J.A., Ketchum K.A.,  
 RA Kimmel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lai Z.,  
 RA Lasko P., Lai Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,  
 RA Liu X., Mattei B., McIntosh T.C., McLeod M.P., McPherson D.,

RA Merkulov G., Milshina N.V., Mobarry C., Morris J., Moshrefi A.,  
 RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,  
 RA Nelson D.R., Nelson K.A., Nixon K., Nusskern D.R., Pacle J.M.,  
 RA Palazzolo M., Pittman G.S., Pan S., Pollard J., Puri V., Reese M.G.,  
 RA Reinert K., Remington K., Saunders R.D.C., Scheeler F., Shen H.,  
 RA Shue B.C., Siden-Kiamos I., Simpson M., Skupski M.P., Smith T.,  
 RA Spier E., Spradling A.C., Stapleton M., Strong R., Sun E.,  
 RA Svirskaas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,  
 RA Wang Z.-Y., Wassarman D.A., Weinstein G.M., Weissbach J.,  
 RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,  
 RA Ye J., Yen R.-F., Zaveri J.S., Zhan M., Zhang G., Zhao Q., Zheng L.,  
 RA Zheng X.H., Zhong F.-N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,  
 RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.;  
 RT "The genome sequence of Drosophila melanogaster.";  
 RL Science 287:2185-2195(2000).  
 RN [4]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN-Oregon-R;  
 RX MEDLINE=20196011; PubMed=10731137;  
 RA Benos P.V., Galt M.K., Ashburner M., Murphy L., Harris D.,  
 RA Barrell B.G., Ferraz C., Vidal S., Brun C., Demallies J., Cadieu E.,  
 RA Dreano S., Gloux S., Lelaure V., Mottier S., Galibert F., Borokova D.,  
 RA Minana B., Kafatos F.C., Louis C., Siden-Kiamos I., Bolshakov S.,  
 RA Papadogiannakis G., Spanos L., Cox S., Madueno E., de Pablos B.,  
 RA Modolell J., Peter A., Schoetler P., Werner M., Mourikoti F.,  
 RA Bellert N., Dowe G., Schaefer U., Jaekle H., Buckleton A.,  
 RA Callister D.M., Campbell L.A., Darlmitou A., Henderson N.S.,  
 RA McMillan P.J., Salles C., Tait E.A., Valenti P., Saunders R.D.C.,  
 RA Clover D.M.;  
 RT "From sequence to chromosome: the tip of the X chromosome of D.  
 RT melanogaster.";  
 RL Science 287:2220-2222(2000).  
 RN [5]  
 RP SEQUENCE OF 2505-2611 FROM N.A.  
 RX MEDLINE=85099329; PubMed=2981631;  
 RA Wharton K.A., Yedvobnick B., Finmerly V.G., Artavanis-Tsakonas S.;  
 RT "opa: a novel family of transcribed repeats shared by the Notch locus  
 RT and other developmentally regulated loci in D. melanogaster.";  
 RL Cell 40:55-62(1985).  
 RN [6]  
 RP SEQUENCE OF 1-8 FROM N.A.  
 RX MEDLINE=87257846; PubMed=3037327;  
 RA Kelley M.R., Kidd S., Berg R.L., Young M.W.;  
 RT "Restriction of P-element insertions at the Notch locus of Drosophila  
 RT melanogaster.";  
 RL Mol. Cell. Biol. 7:1545-1548(1987).  
 RN [7]  
 RP REVIEW.  
 RA Harris W.A.;  
 RT "Many cell types specified by Notch function.";  
 RL Curr. Biol. 1:120-122(1991).  
 RT -1- FUNCTION: Functions as a receptor for membrane-bound ligands Delta  
 and Serrate to regulate cell-fate determination, upon ligand  
 activation through the released notch intracellular domain (NICD)  
 it forms a transcriptional activator complex with Su(H)  
 (Suppressor of hairless) and activates genes of the enhancer of  
 split locus. Essential for proper differentiation of ectoderm.  
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 CC -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
 CC -1- SIMILARITY: CONTAINS 6 ANK REPEATS.  
 CC -1- SIMILARITY: CONTAINS 6 ANK REPEATS.  
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 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 DR EMBL: M16152; AAB59220.1; -;  
 DR EMBL: M16153; AAB59220.1; JOINED.

```

Best Loca Similarity 29.2%; Pred. No. 27;
Matches 7; Conservative 12; Mismatches 5; Indels 0; Gaps 0.

OY 4 XMOXCAQXIDCCSXKXCNXXNXC 27
   :||:||||:||||:|:|:
Db 822 TGQCKETNIDCVTPNCGNGGTCT 845

RESULT 15
NTCA_MOUSE
ID NTCA_MOUSE STANDARD; PRT: 1964 AA.
AC P31695; Q62389; Q62390; Q35442; Q9RIW9; Q88314; Q88316; Q9RIX0;
AD 01-JUL-1993 (Rel. 26, Created)
DT 01-NOV-1993 (Rel. 35, Last sequence update)
DT 15-JUN-2002 (Rel. 41, Last annotation update)
DE Neurogenic locus notch homolog protein 4 precursor (Notch 4)
DE [Contains: Transforming protein Int-3].
GN NOTCH4 OR INT3 OR INT-3.
OS Mus musculus (Mouse).
OC Eumariota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX NCBI_TaxID=10090;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE-92194507; PubMed-1312643;
RA Robbins J., Blondel B.D., Gallahan D., Callahan R.;
RT "Mouse mammary tumor gene int-3: a member of the notch gene family
RT transforms mammary epithelial cells.";
RL J. Virol. 66:2594-2599(1992).
RN [2]
RP REVISIONS. SEQUENCE FROM N.A.
RX MEDLINE-97294599; PubMed-9150355;
RA Gallahan D., Callahan R.;
RT "The mouse mammary tumor associated gene INT3 is a unique member of
RT the NOTCH gene family [NOTCH4].";
RL Oncogene 14:1883-1890(1997).
RN [3]
RP SEQUENCE FROM N.A.
RX TISSUE=Lung, and Testis;
RC MEDLINE-96281668; PubMed-8681805;
RA Uytendaele H., Marazzi G., Wu G., Yan Q., Sassoon D., Kitajewski J.;
RT "Notch4/int-3, a mammary proto-oncogene, is an endothelial
RT cell-specific mammalian Notch gene.";
RL Development 122:2251-2259(1996).
RN [4]
RP SEQUENCE FROM N.A.
RX Rowen L., Malaitas G., Qin S., Ahearn M.E., Dankers C., Laskey S.,
RA Loretz C., Schmidt S., Tipton S., Traicooff R., Zackrone K., Hood L.;
RT "Sequence of the mouse major histocompatibility locus class III
RT region.";
RL Submitted (OCT-1997) to the EMBL/GenBank/DBJ databases.
RN [5]
RP SEQUENCE OF 1436-1600 FROM N.A.
RX MEDLINE-99252212; PubMed-10233982;
RA Lee J.-S., Haruna T., Ishimoto A., Honjo T., Yanagawa S.-I.;
RT "Intracisternal type A particle-mediated activation of the Notch4/int3
RT gene in a mouse mammary tumor: generation of truncated Notch4/int3
RT mRNAs by retroviral splicing events.";
RL J. Virol. 73:5166-5171(1999).
RN [6]
RP FUNCTION.
RX MEDLINE-21244657; PubMed-11344305;
RA Uytendaele H., Ho J., Rossant J., Kitajewski J.;
RT "Vascular patterning defects associated with expression of activated
RT Notch4 in embryonic endothelium.";
RL Proc. Natl. Acad. Sci. U.S.A. 98:5643-5648(2001).
RN [7]
RP SEQUENCE OF 1463-1964, POST-TRANSLATIONAL PROCESSING, AND MUTAGENESIS
RX OF VAL-1463.
RP MEDLINE-21523956; PubMed-11518718;
RA Saxena M.T., Schroeter E.H., Munum J.S., Kopan R.;
RT "Murine notch homologs (NL-4) undergo presenilin-dependent
RT proteolysis.";

```

RL J. Biol. Chem. 276:40268-40273(2001).  
 RN [8]  
 RP POST-TRANSLATIONAL PROCESSING.  
 RX MEDLINE-21374376; PubMed-1145941;  
 RA Mizutani T., Taniguchi Y., Aoki T., Hashimoto N., Honjo T.;  
 RT "Conservation of the biochemical mechanisms of signal transduction  
 among mammalian Notch family members.";  
 RL Proc. Natl. Acad. Sci. U.S.A. 98:9026-9031(2001).  
 CC -1- FUNCTION: Functions as a receptor for membrane-bound ligands  
 Jagged1, Jagged2 and Delta to regulate cell-fate determination.  
 Upon ligand activation through the released notch intracellular  
 domain (NICD) it forms a transcriptional activator complex with  
 RBP-J kappa and activates genes of the enhancer of split locus.  
 Affects the implementation of differentiation, proliferation and  
 apoptotic programs (By similarity). May regulate branching  
 morphogenesis in the developing vascular system.  
 CC -1- SUBUNIT: Heterodimer of a C-terminal fragment N(TM) and a N-  
 terminal fragment N(EC) which are probably linked by disulfide  
 bonds.  
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein. Following  
 proteolytic processing NICD is translocated to the nucleus.  
 CC -1- TISSUE SPECIFICITY: Highly expressed in lung, moderately in heart  
 kidney, and at lower levels in the ovary and skeletal muscle. A  
 very low expression is seen in the brain, intestine, liver and  
 testis.  
 CC -1- DEVELOPMENTAL STAGE: Highly expressed in endothelial cells during  
 embryonic development from 9.0 d.p.c.  
 CC -1- PTM: Synthesized in the endoplasmic reticulum as an inactive form  
 which is proteolytically cleaved by a furin-like convertase in the  
 trans-golgi network before it reaches the plasma membrane to yield  
 an active, ligand-accessible form. Cleavage results in a C-  
 terminal fragment N(TM) and a N-terminal fragment N(EC). Following  
 ligand binding, it is cleaved by TNF-alpha converting enzyme  
 (TACE) to yield a membrane-associated intermediate fragment called  
 notch extracellular truncation (NEXT). This fragment is then  
 cleaved by presenilin dependent gamma-secretase to release a  
 notch-derived peptide containing the intracellular domain (NICD)  
 from the membrane.  
 CC -1- PTM: Phosphorylated.  
 CC -1- DISEASE: Loss of the extracellular domain causes constitutive  
 activation of the Notch protein, which leads to hyperproliferation  
 of glandular epithelial tissues and development of mammary  
 carcinomas.  
 CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 CC -1- SIMILARITY: CONTAINS 29 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
 CC -1- SIMILARITY: CONTAINS 5 ANK REPEATS.  
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 or send an email to [license@isb-slb.ch](mailto:license@isb-slb.ch))  
 CC -----  
 DR EMBL: M80456; AAB38377.1; -;  
 DR EMBL: U43691; AAC52630.1; -;  
 DR EMBL: U43691; AAC52631.1; -;  
 DR EMBL: AF030001; AAB82004.1; -;  
 DR EMBL: AB016771; BAA33281.1; ALT\_SEQ.  
 DR EMBL: AB016772; BAA33283.1; ALT\_INIT.  
 DR EMBL: AB016773; BAA33284.1; ALT\_INIT.  
 DR EMBL: AB016774; BAA33285.1; -;  
 DR PIR: A38072; TVMW3.  
 DR HSSP: P08709; 1BF9.  
 DR MGD: MGI:107471; Notch4.  
 DR InterPro: IPR002110; ANK.  
 DR InterPro: IPR000152; Asx\_hydroxyl.  
 DR InterPro: IPR000561; EGF-like.  
 DR InterPro: IPR000742; EGF-2.  
 DR InterPro: IPR001881; EGF\_Ca.  
 DR InterPro: IPR001438; EGF\_II.

DR InterPro: IPR008800; Notch.  
 DR Pfam: PF00008; EGF; 27.  
 DR Pfam: PF00023; ank; 6.  
 DR Pfam: PF00066; notch; 2.  
 DR PRINTS: PR01415; ANKYRN.  
 DR PRINTS: PR00010; EGRBLOOD.  
 DR PRINTS: PR01452; NOTCH.  
 DR SMART: SM00248; ANK; 5.  
 DR SMART: SM00179; EGF\_CA; 11.  
 DR SMART: SM00001; EGF\_Like; 15.  
 DR SMART: SM00004; NL; 2.  
 DR PROSITE: PS50088; ANK\_REPEAT; 5.  
 DR PROSITE: PS50297; ANK\_REPEAT\_REGION; 1.  
 DR PROSITE: PS00010; ASX\_HYDROXYL; 11.  
 DR PROSITE: PS00022; EGF\_1; 28.  
 DR PROSITE: PS01186; EGF\_2; 21.  
 DR PROSITE: PS01187; EGF\_CA; 9.  
 KW Receptor; Transcription regulation; Activator; Differentiation;  
 KW Developmental protein; Repeat; ANK repeat; EGF-like domain;  
 KW Transmembrane; Glycoprotein; Signal; Phosphorylation; Proto-oncogene.  
 FT SIGNAL 1 20  
 FT CHAIN 21 1964  
 FT CHAIN 1411 1964  
 FT CHAIN 1428 1964  
 FT CHAIN 1463 1964  
 FT DOMAIN 21 1443  
 FT TRANSMEM 1444 1464  
 FT DOMAIN 1465 1964  
 FT DOMAIN 21 60  
 FT DOMAIN 61 112  
 FT DOMAIN 115 152  
 FT DOMAIN 153 189  
 FT DOMAIN 191 229  
 FT DOMAIN 231 271  
 FT DOMAIN 273 309  
 FT DOMAIN 311 350  
 FT DOMAIN 352 388  
 FT DOMAIN 389 427  
 FT DOMAIN 429 470  
 FT DOMAIN 472 508  
 FT DOMAIN 510 546  
 FT DOMAIN 548 584  
 FT DOMAIN 586 622  
 FT DOMAIN 623 656  
 FT DOMAIN 658 686  
 FT DOMAIN 688 724  
 FT DOMAIN 726 762  
 FT DOMAIN 764 800  
 FT DOMAIN 803 839  
 FT DOMAIN 841 877  
 FT DOMAIN 878 924  
 FT DOMAIN 926 962  
 FT DOMAIN 964 1000  
 FT DOMAIN 1002 1040  
 FT DOMAIN 1042 1081  
 FT DOMAIN 1083 1122  
 FT DOMAIN 1126 1167  
 FT REPEAT 1168 1208  
 FT REPEAT 1209 1242  
 FT REPEAT 1243 1282  
 FT REPEAT 1282 1657  
 FT REPEAT 1657 1691  
 FT REPEAT 1691 1724  
 FT REPEAT 1724 1757  
 FT ANK 1.  
 FT ANK 2.  
 FT ANK 3.  
 FT ANK 4.  
 Query Match 54.2%; Score 65; DB 1; Length 1964;  
 Best Local Similarity 33.38; Pred. No. 26;  
 Matches 7; Conservative 12; Mismatches 2; Indels 0; Gaps 0;  
 QY 7 XCXQXLDCCSXCNXKNXCV 27  
 DB 348 GCENLDDCAATCAFGSTCI 368

Search completed: January 14, 2003, 18:31:05  
Job time : 13 secs

\* \* \*

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OM protein - protein search, using sw model

Run on: January 14, 2003, 18:29:32 ; Search time 28 Seconds

(without alignments)  
198.688 Million cell updates/sec

Title: US-09-666-837b-1  
Perfect score: 120  
Sequence: 1 CXIXNKCXQXLDCCSXXCXNXCVCV 27

Scoring table: BLOSUM62DX  
Gapop 10.0 , Gapext 0.5

Searched: 671580 seqs, 206047115 residues  
Total number of hits satisfying chosen parameters: 671580

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database :

1: sp.archaea:\*  
2: sp.bacteria:\*  
3: sp.fungi:\*  
4: sp.human:\*  
5: sp.invertebrate:\*  
6: sp.mammal:\*  
7: sp.mhc:\*  
8: sp.organelle:\*  
9: sp.phage:\*  
10: sp.plant:\*  
11: sp rodent:\*  
12: sp\_virus:\*  
13: sp vertebrate:\*  
14: sp\_unclassified:\*  
15: sp\_rvirus:\*  
16: sp\_bacteriap:\*  
17: sp\_archaeap:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

#### SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	55.8	778	13	Q9IBG4	Q9IBG4 xenopus lae
2	55.8	2146	5	Q9VC97	Q9VC97 drosophila
3	55.0	664	3	Q9IAR6	Q9IAR6 brachydanio
4	55.0	721	13	Q9I902	Q9I902 xenopus lae
5	55.0	1551	5	Q9NGV4	Q9NGV4 drosophila
6	55.0	2447	13	Q13149	Q13149 fugu rubrip
7	55.0	3396	5	Q9YMS5	Q9YMS5 drosophila
8	54.2	752	13	Q42374	Q42374 brachydanio
9	54.2	1075	5	Q9NC90	Q9NC90 strongyloce
10	54.2	1214	13	Q90YD2	Q90YD2 xenopus lae
11	54.2	1290	13	Q9W6E1	Q9W6E1 gallus gall
12	54.2	1440	5	Q20204	Q20204 caenorhabdi
13	54.2	2531	5	Q16004	Q16004 lytechinus
14	54.2	2653	5	Q25253	Q25253 lucilia cup
15	53.3	838	5	Q9VQAG	Q9VQAG drosophila
16	53.3	1372	5	P91526	P91526 caenorhabdi

17	64	53.3	2352	5	Q61240	Q61240 halocynthia
18	64	53.3	3623	11	Q70244	Q70244 rattus norv
19	63	52.5	642	13	P79941	P79941 xenopus lae
20	63	52.5	1687	11	Q61204	Q61204 mus musculu
21	62	51.7	153	10	Q9AUD1	Q9AUD1 sesamum ind
22	62	51.7	204	4	Q9BQ54	Q9BQ54 homo sapien
23	62	51.7	713	5	Q962W9	Q962W9 podocoryne
24	62	51.7	723	4	Q9UJV2	Q9UJV2 homo sapien
25	62	51.7	723	4	Q9NU41	Q9NU41 homo sapien
26	62	51.7	1515	13	Q9PD37	Q9PD37 brachydanio
27	62	51.7	1685	5	Q9U4A2	Q9U4A2 plasmodium
28	62	51.7	2524	5	Q9GPA5	Q9GPA5 brachyosto
29	61.5	51.2	81	5	Q9BP77	Q9BP77 conus arena
30	61.5	51.2	471	10	Q8VZ55	Q8VZ55 arabidopsis
31	61.5	51.2	481	10	Q9ZV77	Q9ZV77 arabidopsis
32	61	50.8	66	5	Q9M6P8	Q9M6P8 conus catus
33	61	50.8	66	5	Q9NCW0	Q9NCW0 conus catus
34	61	50.8	66	5	Q9NCV9	Q9NCV9 conus catus
35	61	50.8	463	10	Q9AMX7	Q9AMX7 oryza sativ
36	61	50.8	530	5	Q24526	Q24526 drosophila
37	61	50.8	728	13	Q90656	Q90656 gallus gall
38	61	50.8	1025	11	Q9Z166	Q9Z166 mus musculu
39	61	50.8	1216	13	Q90Y55	Q90Y55 brachydanio
40	61	50.8	1254	13	Q9YHU2	Q9YHU2 brachydanio
41	61	50.8	1254	13	Q90Y56	Q90Y56 brachydanio
42	61	50.8	1316	4	Q96J07	Q96J07 homo sapien
43	61	50.8	1404	5	Q9VB65	Q9VB65 drosophila
44	61	50.8	1480	5	Q9V7P8	Q9V7P8 drosophila
45	61	50.8	1504	5	Q9XYV4	Q9XYV4 drosophila

#### ALIGNMENTS

RESULT 1  
Q9IBG4 PRELIMINARY: PRT: 778 AA.  
ID Q9IBG4  
AC Q9IBG4;  
DT 01-OCT-2000 (TREMBLrel. 15, Created)  
DR 01-OCT-2000 (TREMBLrel. 15, Last sequence update)  
DT 01-DEC-2001 (TREMBLrel. 19, Last annotation update)  
DE Secretory protein containing EGF domain precursor.  
OS Xenopus laevis (African clawed frog).  
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipidoidea; Pipidae;  
OC Xenopodinae; Xenopus.  
OX NCBI\_TaxID=8355;  
RN [1]  
RP SEQUENCE FROM N.A.  
RX MEDLINE=20245325; PubMed=10781962;  
RA Kuriyama S., Miyatani S., Kinoshita T.;  
RT "Xerl; a novel secretory protein expressed in eye and brain of Xenopus  
embryo.";  
RT Mech. Dev. 93:233-237(2000).  
DR EMBL: AB027453; BAA95001.1; -.  
DR HSSP: P08709; IBE9.  
DR InterPro: IPR000152; Asx\_Hydroxyl.  
DR InterPro: IPR000561; EGF-like.  
DR InterPro: IPR000742; EGF\_2.  
DR InterPro: IPR001881; EGF\_Ca.  
DR InterPro: IPR001438; EGF\_T1.  
DR InterPro: IPR002049; Laminin\_EGF.  
DR InterPro: IPR001791; Laminin\_G.  
DR Pfam: PF00008; EGF\_13.  
DR PRINTS: PR00054; Laminin\_G; 1.  
DR PRINTS: PR00011; EGF\_LAMININ.  
DR SMART: SM00179; EGF\_CA; 6.  
DR SMART: SM00282; EGF\_Like; 7.  
DR PROSITE: PS00010; ASX\_HYDROXYL; UNKNOWN\_7.  
DR PROSITE: PS00022; EGF\_1; UNKNOWN\_10.  
DR PROSITE: PS01186; EGF\_2; 10.







DR InterPro: IPR000561; EGF-like.  
 DR InterPro: IPR000742; EGF\_2.  
 DR InterPro: IPR001881; EGF\_CA.  
 DR InterPro: IPR001438; EGF\_11.  
 DR InterPro: IPR000083; Fibronctn1.  
 DR InterPro: IPR002049; Lamlnin\_EGF.  
 DR InterPro: IPR000800; Notch.  
 DR Pfam: PF000023; ank; 6.  
 DR Pfam: PF00008; EGF\_35.  
 DR Pfam: PF00066; notch; 3.  
 DR PRINTS: PR00010; EGFBL00D.  
 DR PRINTS: PR00011; EGFBLAMIN.  
 DR PRINTS: PR00012; ENTPEI.  
 DR SMART: SM00248; ANK; 5.  
 DR SMART: SM00179; EGF\_CA; 20.  
 DR SMART: SM00001; EGF\_Like; 14.  
 DR SMART: SM00004; NL; 3.  
 DR PROSITE: PS50088; ANK\_REPEAT; 8.  
 DR PROSITE: PS50297; ANK\_REPEAT\_REGION; 2.  
 DR PROSITE: PS00010; ASX\_HYDROXYL; 22.  
 DR PROSITE: PS00022; EGF\_1; UNKNOWN\_35.  
 DR PROSITE: PS01186; EGF\_2; 29.  
 DR PROSITE: PS01187; EGF\_CA; 20.  
 DR ANK repeat; Calcium-binding; EGF-like domain; Glycoprotein;  
 KM Hydroxylation; Repeat.  
 FT NON\_TER  
 SQ SEQUENCE 2447 AA; 262541 MW; 1A8E2A372A085D84 CRC64;

Query Match 55.0%; Score 66; DB 13; Length 2447;  
 Best Local Similarity 29.0%; Pred. No. 6.2;  
 Matches 9; Conservative 15; Mismatches 3; Indels 4; Gaps 1;

Qy 1 CXIXN---OXCXQXLDCCSXXCNXXNCV 27  
 Db 279 CVCVNGMSGDCCSENIDCDTACSPSTCV 309

RESULT 7  
 Q9VMS5 PRELIMINARY; PRT; 3396 AA.  
 AC Q9VMS5;  
 DT 01-MAY-2000 (TREMBLrel. 13, Created)  
 DT 01-MAY-2000 (TREMBLrel. 13, Last sequence update)  
 DT 01-JUN-2000 (TREMBLrel. 21, Last annotation update)  
 DE CG9138 protein.  
 GN SP1070 OR CG9138.  
 OS Drosophila melanogaster (Fruit fly).  
 OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;  
 OC Pterygota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;  
 OC Ephydroidea; Drosophilidae; Drosophila.  
 OC NCBI\_Taxid=7227;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN=BERKELEY;  
 RA MEDLINE=20196006; Pubmed=10711132;  
 RA Adams M.D., Celniker S.E., Holt R.A., Evans C.A., Gocayne J.D.,  
 RA Amanatides P.G., Scherer S.E., Li P.W., Hoskins R.A., Galle R.F.,  
 RA George R.A., Lewis S.E., Richards S., Ashburner M., Henderson S.N.,  
 RA Sutton G.G., Wortman J.R., Yandell M.D., Zhang Q., Chen L.X.,  
 RA Brandon R.C., Rogers Y.-H.C., Blazer R.G., Champe M., Pfeiffer B.D.,  
 RA Wan K.H., Doyle C., Baxter E.G., Helt G., Nelson C.R., Miklos G.L.G.,  
 RA Abbill J.F., Agbayani A., An H.-J., Andrews-Pfannkoch C., Baldwin D.,  
 RA Ballew R.M., Basu A., Baxendale J., Bayraktaroglu L., Beasley E.M.,  
 RA Beeson K.Y., Benos P.V., Berman B.P., Bhandari D., Bolshakov S.,  
 RA Botkova D., Botchan M.R., Bouck J., Brokstein P., Brottler P.,  
 RA Butlis K.C., Busam D.A., Butler H., Cadien E., Center A., Chandra I.,  
 RA Cherry J.M., Cawley S., Dahlke C., Davenport L.B., Davies P.,  
 RA de Pablos B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,  
 RA Dodson K., Doup L.E., Downes M., Dugan-Rocha S., Dunkov B.C., Dunn P.,  
 RA Durbin K.J., Evangelista C.C., Ferraz C., Ferriera S., Fleischmann W.,  
 RA Fogler C., Gabrielian A.E., Garg N.S., Gelbart W.M., Glasser K.,  
 RA Glodok A., Gong F., Gorrell J.H., Gu Z., Guan P., Harris M.,  
 RA Harris N.L., Harvey D., Heiman T.J., Hernandez J.R., Houck J.,

RA Hostin D., Houston K.A., Howland T.J., Wei M.-H., Ibegwam C.,  
 RA Jatali M., Kalush F., Karpen G.H., Ke Z., Kennison J.A., Ketchum K.A.,  
 RA Kimmel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lal Z.,  
 RA Lasko P., Lei Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,  
 RA Liu X., Maltel B., McInosh T.C., McLeod K.P., McInosh D.,  
 RA Merkulov G., Mishina N.V., Mobarry C., Morris J., Moshrefi A.,  
 RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,  
 RA Nelson D.R., Nelson K.A., Nixon K., Nuskern D.R., Pacled J.M.,  
 RA Palazolo M., Pittman G.S., Pan S., Pollard J., Puri V., Reese M.G.,  
 RA Reinert K., Remington K., Saunders R.D.C., Scheeler F., Shen H.,  
 RA Shue B.C., Siden-Klamos I., Simpson M., Skupski M.P., Smith T.,  
 RA Spier E., Spradling A.C., Stapleton M., Strong R., Sun E.,  
 RA Svirskas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,  
 RA Wang Z.-Y., Wasserman D.A., Weinstein G.M., Weissbach J.,  
 RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,  
 RA Ye J., Yeh R.-F., Zaveri J.S., Zhan M., Zhang G., Zhao Q., Zheng L.,  
 RA Zheng X.H., Zhong F.N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,  
 RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.;  
 RT "The genome sequence of Drosophila melanogaster."  
 RL Science 287:2185-2195(2000).  
 CC -1- SIMILARITY: CONTAINS 3 CUB DOMAINS.  
 DR EMBL: AE003615; AAF52472.1; -.  
 DR HSP; P00740; IEDM.  
 DR Flybase: FBgn0031879; SP1070.  
 DR InterPro: IPR000152; Asx\_hydroxyl.  
 DR InterPro: IPR000859; CUB domain.  
 DR InterPro: IPR000561; EGF-like.  
 DR InterPro: IPR000742; EGF\_2.  
 DR InterPro: IPR001881; EGF\_CA.  
 DR InterPro: IPR001438; EGF\_11.  
 DR InterPro: IPR000421; FA58\_C.  
 DR InterPro: IPR001092; HLB\_basic.  
 DR InterPro: IPR003410; Hyalin.  
 DR InterPro: IPR001791; Lamlnin-G.  
 DR InterPro: IPR002172; LDL\_recept-A.  
 DR InterPro: IPR000436; Sush1\_SCR\_CCP.  
 DR InterPro: IPR001368; TNER\_C6.  
 DR Pfam: PF00431; CUB; 3.  
 DR Pfam: PF00008; EGF; 17.  
 DR Pfam: PF00754; F5\_FB\_type\_C; 2.  
 DR Pfam: PF02494; HVR; 3.  
 DR Pfam: PF00057; Id1\_recept\_a; 1.  
 DR Pfam: PF00084; sush1; 7.  
 DR PRINTS: PR00010; EGFBL00D.  
 DR SMART: SM00032; CCP; 8.  
 DR SMART: SM00042; CUB; 3.  
 DR SMART: SM000179; EGF\_CA; 8.  
 DR SMART: SM00001; EGF\_Like; 9.  
 DR SMART: SM00231; FA58C; 2.  
 DR SMART: SM00192; LamG; 1.  
 DR SMART: SM00192; LDLa; 1.  
 DR SMART: SM00208; TNER; 2.  
 DR PROSITE: PS00010; ASX\_HYDROXYL; 11.  
 DR PROSITE: PS01180; CUB; 6.  
 DR PROSITE: PS00022; EGF\_1; 15.  
 DR PROSITE: PS01186; EGF\_2; 13.  
 DR PROSITE: PS01187; EGF\_CA; 7.  
 DR PROSITE: PS01285; FA58C\_1; 1.  
 DR PROSITE: PS01209; LDLRA\_1; 1.  
 DR PROSITE: PS50068; LDLRA\_2; 2.  
 KW Calcium-binding; EGF-like domain; Glycoprotein; Hydroxylation; Repeat.  
 SQ SEQUENCE 3396 AA; 369389 MW; B618E9ACEA13E0E5 CRC64;

Query Match 55.0%; Score 66; DB 5; Length 3396;  
 Best Local Similarity 33.3%; Pred. No. 8.3;  
 Matches 8; Conservative 11; Mismatches 5; Indels 0; Gaps 0;

Qy 4 XNQCXQXLDCCSXXCNXXNCV 27  
 Db 2119 TGKNCQHTIDCCSNPCGAGATCV 2142

RESULT 8

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042374
ID 042374 PRELIMINARY; PRT: 752 AA.
AC 042374;
DT 01-JAN-1998 (TREMBLrel. 05, Created)
DT 01-JAN-1998 (TREMBLrel. 05, Last sequence update)
DT 01-MAR-2002 (TREMBLrel. 20, Last annotation update)
DE Notch receptor protein (Fragment).
GN NOTCH2 OR NOTCH6.
OS Brachydanio rerio (Zebrafish) (Zebra danio).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC Cyprinidae; Danio.
OX NCBI_TaxID=7955;
RN [1]
RP SEQUENCE FROM N.A.
RA Westin J., Lardelli M.;
RT "Three novel Notch genes in zebrafish: implications for vertebrate
RT Notch gene evolution and function.";
RL Dev. Genes Evol. 207:51-63(1997).
DR EMBL: Y10354; CAA71380.1; -.
DR HSSP: P00740; 1EDM.
DR ZFIN: ZDB-GENE-000329-4; notch2.
DR InterPro: IPR000152; Asx_hydroxyl.
DR InterPro: IPR000561; EGF-like.
DR InterPro: IPR000742; EGF_2.
DR InterPro: IPR001881; EGF_CA.
DR InterPro: IPR001438; EGF_11.
DR InterPro: IPR000083; Fibrinctn1.
DR InterPro: IPR002049; laminin_EGF.
DR InterPro: IPR000800; Notch.
DR Pfam: PF00008; EGF_16.
DR Pfam: PF00066; notch_2.
DR PRINTS: PR00010; EGFL00D.
DR PRINTS: PR00011; EGFLAMININ.
DR PRINTS: PR00012; FNTYPEI.
DR SMART: SM00179; EGF_CA; 9.
DR SMART: SM00001; EGF_Like; 5.
DR SMART: SM00004; NL_2.
DR PROSITE: PS00010; ASX_HYDROXYL; 9.
DR PROSITE: PS00022; EGF_1; UNKNOWN_17.
DR PROSITE: PS01186; EGF_2; 15.
DR PROSITE: PS01187; EGF_CA; 7.
DR Calcium-binding; EGF-like domain; Glycoprotein; Hydroxylation;
KW Receptor; Repeat.
FT NON_TER 1
FT NON_TER 752
SQ SEQUENCE 752 AA; 82103 MW; 30939E16E0327F8A CRC64;

Query Match 54.2%; Score 65; DB 13; Length 752;
Best local Similarity 33.3%; Pred. No. 2.9;
Matches 8; Conservative 10; Mismatches 6; Indels 0; Gaps 0;

QY 4 XNQCXQXLDCCSXKXNKNXCV 27
Db 132 SGDNQCTHIDCSSNFCRNGTCV 155

RESULT 9
Q9NC90 PRELIMINARY; PRT: 1075 AA.
AC Q9NC90;
DT 01-OCT-2000 (TREMBLrel. 15, Created)
DT 01-OCT-2000 (TREMBLrel. 15, Last sequence update)
DT 01-JUN-2002 (TREMBLrel. 21, Last annotation update)
DE Scavenger receptor cysteine-rich protein variant 1.
OS Strongylocentrotus purpuratus (Purple sea urchin).
OC Eukaryota; Metazoa; Echinodermata; Eleutherozoa; Echinozoa;
OC Echinoidea; Euechinozoa; Echinacea; Echinoida; Strongylocentrotidae;
OC Strongylocentrotus.
OX NCBI_TaxID=7668;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=20542095; PubMed=11069281;

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RA Paner Z.;
RT "Dynamic expression of multiple scavenger receptor cysteine-rich genes
RT in coelomocytes of the purple sea urchin.";
RL Proc. Natl. Acad. Sci. U.S.A. 97:13156-13161(2000).
DR EMBL: AF228824; AAF76316.1; -.
DR HSSP: P00740; 1EDM.
DR InterPro: IPR000152; Asx_hydroxyl.
DR InterPro: IPR000561; EGF-like.
DR InterPro: IPR000742; EGF_2.
DR InterPro: IPR001881; EGF_CA.
DR InterPro: IPR001438; EGF_11.
DR InterPro: IPR001190; Srcr_receptor.
DR InterPro: IPR000436; Sushi_SCR_CCP.
DR Pfam: PF00008; EGF_3.
DR Pfam: PF00530; SRCR_7.
DR Pfam: PF00084; sushi_1.
DR PRINTS: PR00010; EGFL00D.
DR PRINTS: PR00258; SPERACTRCPTR.
DR SMART: SM00032; CCP_1.
DR SMART: SM00179; EGF_CA; 2.
DR SMART: SM00001; EGF_Like; 1.
DR SMART: SM00202; SR_6.
DR PROSITE: PS00010; ASX_HYDROXYL; UNKNOWN_2.
DR PROSITE: PS00022; EGF_1; UNKNOWN_2.
DR PROSITE: PS01186; EGF_2; 3.
DR PROSITE: PS01187; EGF_CA; UNKNOWN_1.
DR PROSITE: PS00420; SRCR_1; UNKNOWN_3.
DR PROSITE: PS0287; SRCR_2; 7.
KW EGF-like domain; Glycoprotein; Receptor.
SQ SEQUENCE 1075 AA; 116178 MW; 61395AD6FD30BA3D CRC64;

Query Match 54.2%; Score 65; DB 5; Length 1075;
Best local Similarity 33.3%; Pred. No. 4;
Matches 8; Conservative 10; Mismatches 6; Indels 0; Gaps 0;

QY 4 XNQCXQXLDCCSXKXNKNXCV 27
Db 862 TGSSCDTEIDCSSSPGDNQVCV 885

RESULT 10
Q90YD2 PRELIMINARY; PRT: 1214 AA.
AC Q90YD2;
DT 01-DEC-2001 (TREMBLrel. 19, Created)
DT 01-DEC-2001 (TREMBLrel. 19, Last sequence update)
DT 01-JUN-2002 (TREMBLrel. 21, Last annotation update)
DE X-serrate-1 protein.
GN X-SERRATE-1.
OS Xenopus laevis (African clawed frog).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipidae; Pipidae;
OC Xenopodinae; Xenopus.
OX NCBI_TaxID=8355;
RN [1]
RP SEQUENCE FROM N.A.
RX MEDLINE=21541033; PubMed=11685570;
RA Kiyota T., Jono H., Kuriyama S., Hasegawa K., Miyatani S.,
RA Kinoshita T.;
RT "X-serrate-1 is involved in primary neurogenesis in Xenopus laevis in
RT a complementary manner with X-Delta-1.";
RL Dev. Genes Evol. 211:367-376(2001).
DR EMBL: AB027537; BAB59049.1; -.
DR InterPro: IPR000152; Asx_hydroxyl.
DR InterPro: IPR001774; DSL.
DR InterPro: IPR000561; EGF_Like.
DR InterPro: IPR000742; EGF_2.
DR InterPro: IPR001881; EGF_CA.
DR InterPro: IPR001007; VWF_C.
DR Pfam: PF01414; DSL; 1.
DR Pfam: PF00008; EGF_14.
DR PROSITE: PS00010; ASX_HYDROXYL; UNKNOWN_10.
DR PROSITE: PS00022; EGF_1; UNKNOWN_16.

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Best Local Similarity 26.9%; Pred. No. 5.2;  
Matches 7; Conservative 13; Mismatches 6; Indels 0; Gaps 0;

OY 2 XIXNQXOXHLDCCSXCNXXNXCVCV 27  
DB 938 GFGDGYCEKNIDCVNCKENGKCV 963

RESULT 13

016004 ID 016004 PRELIMINARY; PRT; 2531 AA.  
AC 016004:  
DT 01-JAN-1998 (TREMBLrel. 05, Created)  
DT 01-JAN-1998 (TREMBLrel. 05, Last sequence update)  
DT 01-DEC-2001 (TREMBLrel. 19, Last annotation update)  
DE Notch homolog.  
OS Lytechinus variegatus (Sea urchin).  
OC Eukaryota; Metazoa; Echinodermata; Eleutherozoa; Echinozoa;  
OC Echinozoa; Echinodermata; Echinacea; Temnopneustidae;  
OC Lytechinus.  
OX NCBI\_Taxid=7654;  
RN [1]  
RX MEDLINE=97454256; PubMed=9310331;  
RA Sherwood D.R., McClay D.R.;  
RT "Identification and localization of a sea urchin Notch homologue:  
RT insights into vegetal plate regionalization and Notch receptor  
RT regulation.";  
RT Development 124:3363-3374(1997).  
DR EMBL; AF000634; AAB82088.1; .  
DR HSSP; P01132; 1EGF.  
DR InterPro; IPR002110; ANK.  
DR InterPro; IPR000152; Asx\_hydroxyl.  
DR InterPro; IPR000561; EGF-like.  
DR InterPro; IPR000742; EGF\_2.  
DR InterPro; IPR001881; EGF\_CA.  
DR InterPro; IPR001438; EGF\_11.  
DR InterPro; IPR000600; Notch.  
DR Pfam; PF000023; ank; 6.  
DR Pfam; PF00008; EGF; 35.  
DR Pfam; PF00066; notch; 3.  
DR PRINTS; PR0145; ANKYRIN.  
DR PRINTS; PR0145; ANKYRIN.  
DR PRINTS; PR0145; EGFBLD.  
DR PRINTS; PR0145; NOTCH.  
DR SMART; SM00248; ANK; 5.  
DR SMART; SM00179; EGF\_CA; 23.  
DR SMART; SM00001; EGF\_like; 11.  
DR SMART; SM00004; NL; 3.  
DR PROSITE; PS50088; ANK\_REPEAT; 10.  
DR PROSITE; PS50297; ANK\_REPEAT\_REGION; 2.  
DR PROSITE; PS00010; ASX\_HYDROXYL; 21.  
DR PROSITE; PS00022; EGF\_1; UNKNOWN\_33.  
DR PROSITE; PS01186; EGF\_2; 25.  
DR PROSITE; PS01187; EGF\_CA; 20.  
DR ANK repeat; Calcium-binding; EGF-like domain; Glycoprotein;  
KW Hydroxylation; Repeat.  
SQ SEQUENCE 2531 AA; 273982 MW; 5BF42BEC627CA303 CRC64;

Query Match 54.2%; Score 65; DB 5; Length 2511;  
Best Local Similarity 38.1%; Pred. No. 8.5;  
Matches 8; Conservative 11; Mismatches 2; Indels 0; Gaps 0;

OY 7 KXCXQXLDCCSXCNXXNXCVCV 27  
DB 661 NCEEDIDCESRCHNGTCV 681

RESULT 14

025253 ID 025253 PRELIMINARY; PRT; 2653 AA.  
AC 025253:  
DT 01-NOV-1996 (TREMBLrel. 01, Created)  
DT 01-NOV-1996 (TREMBLrel. 01, Last sequence update)

DT 01-DEC-2001 (TREMBLrel. 19, Last annotation update)  
DE Notch homolog scalloped wings (SCL).  
GN SCL.  
OS Lucilia cuprina (Greenbottle fly) (Australian sheep blowfly).  
OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;  
OC Pterygota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;  
OC Oestroidea; Calliphoridae; Lucilia.  
OX NCBI\_Taxid=7375;  
RN [1]  
RX MEDLINE=96400928; PubMed=8807304;  
RA Davies A.G., Game A.Y., Chen Z., Williams T.J., Goodall S., Yen J.L.,  
RA McKenzie J.A., Batterham P.;  
RT "Scalloped wings is the Lucilia cuprina Notch homologue and a  
RT candidate for the modifier of fitness and asymmetry of diazonia  
RT resistance.";  
RT Genetics 143:1321-1337(1996).  
RN [2]  
RX MEDLINE=97454256; PubMed=9310331;  
RA Sherwood D.R., McClay D.R.;  
RT "Identification and localization of a sea urchin Notch homologue:  
RT insights into vegetal plate regionalization and Notch receptor  
RT regulation.";  
RT Development 124:3363-3374(1997).  
DR EMBL; AF000634; AAB82088.1; .  
DR HSSP; P01132; 1EGF.  
DR InterPro; IPR002110; ANK.  
DR InterPro; IPR000152; Asx\_hydroxyl.  
DR InterPro; IPR000561; EGF-like.  
DR InterPro; IPR000742; EGF\_2.  
DR InterPro; IPR001881; EGF\_CA.  
DR InterPro; IPR001438; EGF\_11.  
DR InterPro; IPR000600; Notch.  
DR Pfam; PF000023; ank; 6.  
DR Pfam; PF00008; EGF; 35.  
DR Pfam; PF00066; notch; 3.  
DR PRINTS; PR0145; ANKYRIN.  
DR PRINTS; PR0145; ANKYRIN.  
DR PRINTS; PR0145; EGFBLD.  
DR SMART; SM00248; ANK; 5.  
DR SMART; SM00179; EGF\_CA; 23.  
DR SMART; SM00001; EGF\_like; 11.  
DR SMART; SM00004; NL; 3.  
DR PROSITE; PS50088; ANK\_REPEAT; 10.  
DR PROSITE; PS50297; ANK\_REPEAT\_REGION; 2.  
DR PROSITE; PS00010; ASX\_HYDROXYL; 21.  
DR PROSITE; PS00022; EGF\_1; UNKNOWN\_33.  
DR PROSITE; PS01186; EGF\_2; 25.  
DR PROSITE; PS01187; EGF\_CA; 20.  
DR ANK repeat; Calcium-binding; EGF-like domain; Glycoprotein;  
KW Hydroxylation; Repeat.  
SQ SEQUENCE 2653 AA; 285928 MW; 6AF2A058FEE6C329 CRC64;

Query Match 54.2%; Score 65; DB 5; Length 2653;  
Best Local Similarity 29.2%; Pred. No. 8.9;  
Matches 7; Conservative 12; Mismatches 5; Indels 0; Gaps 0;

OY 4 XNQCXQXLDCCSXCNXXNXCVCV 27  
DB 268 QGKNCEDNIDCPGHLCONGTCTI 291

RESULT 15

09YOA9 ID 09YOA9 PRELIMINARY; PRT; 838 AA.  
AC 09YOA9:

DT 01-MAY-2000 (TReMBLrel. 13, Created)  
 DT 01-MAY-2000 (TReMBLrel. 13, Last sequence update)  
 DT 01-JUN-2001 (TReMBLrel. 17, Last annotation update)  
 DE CG15388 protein.  
 GN CG15388  
 OS Drosophila melanogaster (Fruit fly)  
 OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;  
 OC Pterygota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;  
 OC Ephydroidea; Drosophilidae; Drosophila.  
 OX NCBI\_TaxID:7227;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN-BERKELEY;  
 RX MEDLINE-20196006; PubMed-10731132;  
 RA Adams M.D., Celniker S.E., Holt R.A., Evans C.A., Gocayne J.D.,  
 RA Amanatides P.G., Scherer S.E., Li P.W., Hoskins R.A., Galle R.F.,  
 RA George R.A., Lewis S.E., Richards S., Ashburner M., Henderson S.N.,  
 RA Sutton G.C., Wortman J.R., Yandell M.D., Zhang Q., Chen L.X.,  
 RA Brandon R.C., Rogers Y.-H.C., Blazer R.G., Champe M., Pfeiffer B.D.,  
 RA Wan K.H., Doyle C., Baxter E.G., Helt G., Nelson C.R., Miklos G.L.G.,  
 RA Abell J.F., Agbayani A., An H.-J., Andrews-Pfannkoch C., Baldwin D.,  
 RA Ballew R.M., Basu A., Baxendale J., Bayraktaroglu L., Beasley E.M.,  
 RA Beeson K.Y., Benos P.V., Berman B.P., Bhandari D., Bolshakov S.,  
 RA Botkova D., Botchan M.R., Bouck J., Brokstein P., Brotler P.,  
 RA Burlis K.C., Busam D.A., Butler H., Cadiou E., Center A., Chandra I.,  
 RA Cherry J.M., Cawley S., Dahlke C., Davenport L.B., Davies P.,  
 RA de Pablos B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,  
 RA Dodson K., Doup L.E., Downes M., Dugan-Rocha S., Dunkov B.C., Dunn P.,  
 RA Durbin K.J., Evangelista C.C., Ferraz C., Ferriera S., Fleischmann W.,  
 RA Foster C., Gabriellian A.E., Garg N.S., Gelbart W.M., Glasser K.,  
 RA Glodex A., Gong F., Gorrell J.H., Gu Z., Guan P., Harris M.,  
 RA Harris N.L., Harvey D., Helman T.J., Hernandez J.R., Houck W.,  
 RA Hostin D., Houston K.A., Howland T.J., Wei M.-H., Idegawa C.,  
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 RA Klumel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lai Z.,  
 RA Lasko P., Lei Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,  
 RA Liu X., Mattei B., McIntosh T.C., McLeod M.P., McPherson D.,  
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 RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,  
 RA Nelson D.R., Nelson K.A., Nixon K., Nusskern D.R., Pacle J.M.,  
 RA Palazolo M., Pittman G.S., Pan S., Pollard J., Puri V., Reese M.G.,  
 RA Reinert K., Remington K., Saunders R.D.C., Scheeler F., Shen H.,  
 RA Shue B.C., Siden-Kiamos I., Simpson M., Skupski M.P., Smith T.,  
 RA Spier E., Spradling A.C., Stapleton M., Strong R., Sun E.,  
 RA Svirskas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,  
 RA Wang Z.-Y., Wassarman D.A., Weinstock G.M., Weissenbach J.,  
 RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,  
 RA Ye J., Yeh R.-F., Zaveri J.S., Zhang M., Zhang G., Zhao Q., Zheng L.,  
 RA Zheng X.H., Zhong F.N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,  
 RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.;  
 RT "The genome sequence of *Drosophila melanogaster*.";  
 RL Science 287:2185-2195(2000).  
 DR EMBL: AE003583; AAF51268.1; -.  
 DR HSP: P00740.1EDM.  
 DR FLYBase; FBgn0031414; CG15388.  
 DR InterPro: IPR000152; Asx\_hydroxyl.  
 DR InterPro: IPR000561; EGF-like.  
 DR InterPro: IPR000742; EGF-2.  
 DR InterPro: IPR001881; EGF\_Ca.  
 DR InterPro: IPR001438; EGF\_II.  
 DR InterPro: IPR002965; P\_rich\_extensn.  
 DR Pfam; PF00008; EGF; 5.  
 DR PRINTS; PRO0010; EGFBL00D.  
 DR PRINTS; PRO1217; PRICHEXTNSN.  
 DR SMART; SM00179; EGF\_CA; 3.  
 DR SMART; SM00001; EGF\_like; 2.  
 DR PROSITE; PS00010; ASX\_HYDROXYL; UNKNOWN\_3.  
 DR PROSITE; PS00022; EGF\_1; 5.  
 DR PROSITE; PS01186; EGF\_2; 3.  
 DR PROSITE; PS01187; EGF\_CA; 3.  
 KW Calcium-binding; EGF-like domain; Glycoprotein; Repeat.  
 SO SEQUENCE 838 AA; 87786 MW; A654CDBE4FDF42B0 CRC64;

Query Match 53.3%; Score 64; DB 5; Length 838;  
 Best Local Similarity 28.0%; Pred. No. 4.3;  
 Matches 7; Conservative 13; Mismatches 5; Indels 0; Gaps 0;

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 DB 4 EIKSNCENVEDCMSNPQNGGLC 28

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GenCore version 5.1.3  
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OM protein - protein search, using sw model

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Searched: 908470 seqs, 133250620 residues

Total number of hits satisfying chosen parameters: 908470

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Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

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15: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA1994.DAT:\*  
16: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA1995.DAT:\*  
17: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA1997.DAT:\*  
18: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA1997.DAT:\*  
19: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA1998.DAT:\*  
20: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA1999.DAT:\*  
21: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA2000.DAT:\*  
22: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA2001.DAT:\*  
23: /SIDS2/gcgdata/geneseq/geneseq-emb1/AA2002.DAT:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	129	92.1	27	22	AAU10196
2	129	92.1	27	22	AAU10197
3	129	92.1	27	22	AAU10199
4	129	92.1	27	22	AAU10202
5	129	92.1	27	22	AAU10218
6	127	90.7	27	18	AAK35723
7	125	89.3	27	22	AAU10203
8	125	89.3	27	22	AAU10206
9	125	89.3	27	22	AAU10212
10	124	88.6	27	22	AAU10207

11	124	88.6	27	22	AAU10217	Snail Kappa-conoto
12	123	87.9	27	22	AAU10198	Snail Kappa-conoto
13	123	87.9	27	22	AAU10214	Snail Kappa-conoto
14	122	87.1	27	22	AAU10200	Snail Kappa-conoto
15	122	87.1	27	22	AAU10204	Snail Kappa-conoto
16	122	87.1	27	22	AAU10205	Snail Kappa-conoto
17	122	87.1	27	22	AAU10210	Snail Kappa-conoto
18	122	87.1	27	22	AAU10216	Snail Kappa-conoto
19	120	85.7	27	22	AAU10201	Snail Kappa-conoto
20	120	85.7	27	22	AAU10209	Snail Kappa-conoto
21	120	85.7	27	22	AAU10211	Snail Kappa-conoto
22	120	85.7	27	22	AAU10213	Snail Kappa-conoto
23	120	85.7	27	22	AAU10215	Snail Kappa-conoto
24	120	85.7	27	22	AAU10219	Snail Kappa-conoto
25	118	84.3	27	22	AAU10208	Snail Kappa-conoto
26	100	71.4	27	22	AAU10195	Snail Kappa-conoto
27	66	47.1	27	23	ABB96772	Omega-conopeptide
28	66	47.1	27	23	ABB96874	Omega-conopeptide
29	65	46.4	26	23	ABB96786	Omega-conopeptide
30	65	46.4	27	23	ABB96774	Omega-conopeptide
31	65	46.4	27	23	ABB96846	Omega-conopeptide
32	65	46.4	27	23	ABB96876	Omega-conopeptide
33	65	46.4	72	23	ABB96638	Omega-conopeptide
34	65	46.4	72	23	ABB96666	Omega-conopeptide
35	65	46.4	72	23	ABB96668	Omega-conopeptide
36	64	45.7	26	14	AAK37774	SNX-202. Synthet
37	64	45.7	26	18	AAK39628	SNX-202. Synthet
38	64	45.7	26	18	AAK19570	SNX-202. Synthet
39	64	45.7	26	18	AAK12985	Omega-conopeptide
40	64	45.7	26	19	AAK72625	Omega-conopeptide
41	64	45.7	26	20	AAK55584	Omega-conopeptide
42	64	45.7	26	21	AAK14370	Omega-conopeptide
43	64	45.7	26	22	AAK56466	Omega-conopeptide
44	64	45.7	26	22	AAK19462	Omega-conopeptide
45	63	45.0	26	23	ABB96887	Omega-conopeptide

## ALIGNMENTS

RESULT 1	AAU10196	standard; peptide; 27 AA.
ID	AAU10196;	
XX		
AC	AAU10196;	
XX		
DT	16-JAN-2002 (first entry)	
XX		
DE	Snail Kappa-conotoxin PY1A analogue R18A.	
XX		
KW	Purple cone snail; kappa-conotoxin PY1A analogue; circulatory;	
KW	cardioactive; antilasthmatic; KAP channel activation; cardiac ischemia;	
KW	cerebral ischemia; ocular ischemia; asthma; R18A.	
XX		
OS	Conus purpurascens.	
OS	Synthetic.	
XX		
PH	Key	Location/Qualifiers
FT	Modified-site	4
FT	Modified-site	/note= "Hydroxyproline"
FT	Modified-site	27
FT	/note= "The C-terminus is either a carboxyl group or an amide group"	
XX		
XX	WO200121648-A1.	
PN		
XX		
PD	29-MAR-2001.	
XX		
PF	21-SEP-2000; 2000WO-US25827.	
XX		
PR	22-SEP-1999; 99US-155135P.	
PR	20-JUL-2000; 2000US-0219438.	
XX		

PA (COGN-) COGNETIX INC.  
 XX  
 PI Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
 PI Jones RR;  
 XX  
 DR WPI: 2001-648090/74.  
 XX  
 XX Treating disorders associated with radical depolarization of excitable  
 PT membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
 PT comprises activating a KATP channel by administering to an individual a  
 PT kappa-conotoxin PVIIA peptide -  
 XX  
 PS Claim 1: Page 27: 46pp: English.  
 XX  
 CC The invention relates to treating disorders associated with radical  
 CC depolarisation of excitable membrane by activating a KATP channel  
 CC comprising administering to an individual a kappa-conotoxin PVIIA  
 CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
 CC active salt. The conotoxins are used for treating disorders associated  
 CC with radical depolarisation of excitable membrane by activating a KATP  
 CC channel, especially cardiac ischemia, cerebral ischemia, ocular  
 CC ischemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.  
 XX  
 SQ Sequence 27 AA:

Query Match 92.1%; Score 129; DB 22; Length 27;  
 Best Local Similarity 81.5%; Pred. No. 5.4e-09;  
 Matches 22; Conservative 0; Mismatches 5; Indels 0; Gaps 0;

QY 1 CRINQKCFQHLDDCCSXKXNXXCV 27  
 |||||||  
 DB 1 CRINQKCFQHLDDCCSACNRFNKC 27

## RESULT 2

AAU10197  
 ID AAU10197 standard; peptide: 27 AA.

AC AAU10197;

DT 16-JAN-2002 (first entry)

DE Snail Kappa-conotoxin PVIIA analogue R22A.

KW Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;

KW cardioactive; antiasthmatic; KATP channel activation; cardiac ischemia;

KW cerebral ischemia; ocular ischemia; asthma; R22A.

OS Conus purpurascens.

OS Synthetic.

Key Location/Qualifiers  
 Modified-site 4 /note= "Hydroxyproline"

Modified-site 27 /note= "The C-terminus is either a carboxyl group  
 or an amide group"

WO200121648-A1.

29-MAR-2001.

21-SEP-2000; 2000WO-US25827.

22-SEP-1999; 99US-155135P.

20-JUL-2000; 2000US-0219438.

(COGN-) COGNETIX INC.

Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
 Jones RR;

DR WPI: 2001-648090/74.  
 XX  
 PT Treating disorders associated with radical depolarization of excitable  
 PT membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
 PT comprises activating a KATP channel by administering to an individual a  
 PT kappa-conotoxin PVIIA peptide -  
 XX  
 PS Claim 1: Page 27: 46pp: English.  
 XX  
 CC The invention relates to treating disorders associated with radical  
 CC depolarisation of excitable membrane by activating a KATP channel  
 CC comprising administering to an individual a kappa-conotoxin PVIIA  
 CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
 CC active salt. The conotoxins are used for treating disorders associated  
 CC with radical depolarisation of excitable membrane by activating a KATP  
 CC channel, especially cardiac ischemia, cerebral ischemia, ocular  
 CC ischemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.  
 XX  
 SQ Sequence 27 AA:

Query Match 92.1%; Score 129; DB 22; Length 27;  
 Best Local Similarity 81.5%; Pred. No. 5.4e-09;  
 Matches 22; Conservative 0; Mismatches 5; Indels 0; Gaps 0;

QY 1 CRINQKCFQHLDDCCSXKXNXXCV 27  
 |||||||  
 DB 1 CRINQKCFQHLDDCCSRKCNAFNKC 27

## RESULT 3

AAU10199  
 ID AAU10199 standard; peptide: 27 AA.

AC AAU10199;

DT 16-JAN-2002 (first entry)

DE Snail Kappa-conotoxin PVIIA analogue K19A.

KW Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;

KW cardioactive; antiasthmatic; KATP channel activation; cardiac ischemia;

KW cerebral ischemia; ocular ischemia; asthma; K19A.

OS Conus purpurascens.

OS Synthetic.

Key Location/Qualifiers  
 Modified-site 4 /note= "Hydroxyproline"

Modified-site 27 /note= "The C-terminus is either a carboxyl group  
 or an amide group"

WO200121648-A1.

29-MAR-2001.

21-SEP-2000; 2000WO-US25827.

22-SEP-1999; 99US-155135P.

20-JUL-2000; 2000US-0219438.

(COGN-) COGNETIX INC.

Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
 Jones RR;

WPI: 2001-648090/74.

Treating disorders associated with radical depolarization of excitable  
 PT membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
 PT comprises activating a KATP channel by administering to an individual a



PT kappa-conotoxin PVIIA peptide -  
XX  
XX Claim 1; Page 27; 46pp; English.  
XX  
CC The invention relates to treating disorders associated with radical  
CC depolarisation of excitable membrane by activating a KATP channel  
CC comprising administering to an individual a kappa-conotoxin PVIIA  
CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
CC active salt. The conotoxins are used for treating disorders associated  
CC with radical depolarisation of excitable membrane by activating a KATP  
CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular  
CC ischaemia and asthma. The present sequence is a kappa-conotoxin  
CC PVIIA analogue of the invention.  
XX  
SQ Sequence 27 AA;  
Query Match 92.1%; Score 129; DB 22; Length 27;  
Best Local Similarity 81.5%; Pred. No. 5.4e-09;  
Matches 22; Conservative 0; Mismatches 5; Indels 0; Gaps 0;  
QY 1 CRXNKCFOHLDCCSXKXNXCVCV 27  
1 CRXNKCFOHLDCCSRACNRFNKCVCV 27  
Db  
RESULT 4  
AAU10202  
ID AAU10202 standard; peptide; 27 AA.  
XX  
AC AAU10202;  
XX  
DT 16-JAN-2002 (first entry)  
XX  
DE Snail Kappa-conotoxin PVIIA analogue K25A.  
XX  
KM Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;  
KW cardioactive; antisthmatic; KATP channel activation; cardiac ischaemia;  
KM cerebral ischaemia; ocular ischaemia; asthma; K25A.  
XX  
OS Conus purpurascens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Modified-site 4  
FT Modified-site /note= "Hydroxyproline"  
FT Modified-site 27  
FT /note= "The C-terminus is either a carboxyl group  
or an amide group"  
XX  
PN WO200121648-A1.  
XX  
XX 29-MAR-2001.  
PD  
XX 21-SEP-2000; 2000WO-US25827.  
PF  
XX 22-SEP-1999; 99US-155135P.  
PR 20-JUL-2000; 2000US-0219438.  
XX  
XX (COGN-) COGNETIX INC.  
XX  
PI Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
PI Jones RR;  
XX  
XX WPI; 2001-648090/74.  
DR  
XX  
XX Treating disorders associated with radical depolarization of excitable  
PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma  
PT comprises activating a KATP channel by administering to an individual a  
PT kappa-conotoxin PVIIA peptide -  
XX  
XX Claim 1; Page 27; 46pp; English.  
PS  
XX The invention relates to treating disorders associated with radical

CC depolarisation of excitable membrane by activating a KATP channel  
CC comprising administering to an individual a kappa-conotoxin PVIIA  
CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
CC active salt. The conotoxins are used for treating disorders associated  
CC with radical depolarisation of excitable membrane by activating a KATP  
CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular  
CC ischaemia and asthma. The present sequence is a kappa-conotoxin  
CC PVIIA analogue of the invention.  
XX  
SQ Sequence 27 AA;  
Query Match 92.1%; Score 129; DB 22; Length 27;  
Best Local Similarity 81.5%; Pred. No. 5.4e-09;  
Matches 22; Conservative 0; Mismatches 5; Indels 0; Gaps 0;  
QY 1 CRXNKCFOHLDCCSXKXNXCVCV 27  
1 CRXNKCFOHLDCCSRACNRFNACVCV 27  
Db  
RESULT 5  
AAU10218  
ID AAU10218 standard; peptide; 27 AA.  
XX  
AC AAU10218;  
XX  
DT 16-JAN-2002 (first entry)  
XX  
DE Snail Kappa-conotoxin PVIIA analogue 04A.  
XX  
KM Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;  
KW cardioactive; antisthmatic; KATP channel activation; cardiac ischaemia;  
KM cerebral ischaemia; ocular ischaemia; asthma; 04A.  
XX  
OS Conus purpurascens.  
OS Synthetic.  
XX  
FH Key Location/Qualifiers  
FT Modified-site 4  
FT Modified-site /note= "Hydroxyproline"  
FT Modified-site 27  
FT /note= "The C-terminus is either a carboxyl group  
or an amide group"  
XX  
PN WO200121648-A1.  
XX  
XX 29-MAR-2001.  
PD  
XX 21-SEP-2000; 2000WO-US25827.  
PF  
XX 22-SEP-1999; 99US-155135P.  
PR 20-JUL-2000; 2000US-0219438.  
XX  
XX (COGN-) COGNETIX INC.  
XX  
PI Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
PI Jones RR;  
XX  
XX WPI; 2001-648090/74.  
DR  
XX  
XX Treating disorders associated with radical depolarization of excitable  
PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma  
PT comprises activating a KATP channel by administering to an individual a  
PT kappa-conotoxin PVIIA peptide -  
XX  
XX Claim 1; Page 28; 46pp; English.  
PS  
XX The invention relates to treating disorders associated with radical  
CC depolarisation of excitable membrane by activating a KATP channel  
CC comprising administering to an individual a kappa-conotoxin PVIIA  
CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
CC active salt. The conotoxins are used for treating disorders associated  
CC with radical depolarisation of excitable membrane by activating a KATP

CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular  
 CC ischaemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.

XX  
 SQ Sequence 27 AA;

Query Match

Best Local Similarity 77.8%; Score 129; DB 22; Length 27;

Matches 21; Conservative 0; Mismatches 6; Indels 0; Gaps 0;

OY 1 CRINQKCFQHLDDCCSXKCNXNCV 27  
 ||| ||||| ||| |||

DB 1 CRINQKCFQHLDDCCSRKCNRFNKCVCV 27

RESULT 6

AAW35723 standard; peptide; 27 AA.

XX  
 AC AAW35723;

XX  
 DT 03-APR-1998 (first entry)

XX  
 DE Kappa-conotoxin PVIIA.

XX  
 KW Kappa-conotoxin PVIIA; potassium channel; neurotransmitter release;  
 KW cone snail; venom; goldfish; delta-conotoxin PVIIA; disulphide.

XX  
 OS Conus purpurascens.

XX  
 FH Key Location/Qualifiers

FT Modified-site 4 /note= "optionally 4-trans-hydroxyproline,  
 FT hydroxyproline or proline"

FT Disulphide-bond 1..16 /note= "disulphide bond"

FT Disulphide-bond 8..20 /note= "disulphide bond"

FT Disulphide-bond 15..26 /note= "disulphide bond"

XX  
 PN W09734925-A1.

XX  
 PD 25-SEP-1997.

XX  
 PE 14-MAR-1997; 97WO-US03483.

XX  
 PR 18-MAR-1996; 96US-0619936.

XX  
 PA (UTAH ) UNIV UTAH RES FOUND.

XX  
 PI Grille MM, Olivera BM, Shon K, Terlau H;

XX  
 DR WPI; 1997-480162/44.

XX  
 PT New kappa-conotoxin peptides - which target potassium channels and  
 PT can be used to augment neurotransmitter release in e.g. autoimmune  
 PT diseases.

XX  
 PS Claim 1; Page 23; 29pp; English.

XX  
 CC The present sequence represents a new kappa-conotoxin PVIIA which  
 CC targets potassium channels and can be used to augment neurotransmitter  
 CC release in pathological situations such as autoimmune diseases, e.g.  
 CC Alzheimer's disease, Lambert-Eaton syndrome or myasthenia gravis.

XX  
 CC This peptide together with delta-conotoxin PVIIA act synergistically to  
 CC rapidly immobilize fish which are injected with the two peptides.

XX  
 CC Injection of kappa-conotoxin PVIIA alone results in different symptoms  
 CC with an injected fish becoming hyperactive and then contracting and  
 CC suddenly extending all major fins. This "fin-popping" occurs repeatedly  
 CC resulting in a series of jerky movements, but injection of only  
 CC kappa-conotoxin PVIIA does not immobilize or kill the fish.

SQ Sequence 27 AA;

Query Match

Best Local Similarity 77.8%; Score 127; DB 18; Length 27;

Matches 21; Conservative 0; Mismatches 6; Indels 0; Gaps 0;

OY 1 CRINQKCFQHLDDCCSXKCNXNCV 27  
 ||| ||||| ||| |||

DB 1 CRINQKCFQHLDDCCSRKCNRFNKCVCV 27

RESULT 7

AAU10203 standard; peptide; 27 AA.

XX  
 AC AAU10203;

XX  
 DT 16-JAN-2002 (first entry)

XX  
 DE Snail Kappa-conotoxin PVIIA analogue R2K.

XX  
 KW Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;

XX  
 KW cardioactive; antispasmodic; KATP channel activation; cardiac ischaemia;

XX  
 OS Conus purpurascens.

XX  
 OS Synthetic.

XX  
 FH Key Location/Qualifiers

FT Modified-site 4 /note= "Hydroxyproline"

FT Modified-site 27 /note= "The C-terminus is either a carboxyl group  
 FT or an amide group"

XX  
 PN W0200121648-A1.

XX  
 PD 29-MAR-2001.

XX  
 PE 21-SEP-2000; 2000WO-US25827.

XX  
 PR 22-SEP-1999; 99US-155135P.

XX  
 PR 20-JUL-2000; 2000US-0219438.

XX  
 PA (COGN-) COGNETIX INC.

XX  
 PI Cornelli-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;

XX  
 PI Jones RR;

XX  
 DR WPI; 2001-648090/74.

XX  
 PT Treating disorders associated with radical depolarization of excitable  
 PT membrane e.g. cardiac, cerebral and ocular ischaemia and asthma

XX  
 PT comprises activating a KATP channel by administering to an individual a  
 PT kappa-conotoxin PVIIA peptide -

XX  
 PS Claim 1; Page 27; 46pp; English.

XX  
 CC The invention relates to treating disorders associated with radical  
 CC depolarisation of excitable membrane by activating a KATP channel  
 CC comprising administering to an individual a kappa-conotoxin PVIIA  
 CC (kappa-PVIIA) peptide or its analogue, derivative or physiologically  
 CC active salt. The conotoxins are used for treating disorders associated  
 CC with radical depolarisation of excitable membrane by activating a KATP  
 CC channel, especially cardiac ischaemia, cerebral ischaemia, ocular  
 CC ischaemia and asthma. The present sequence is a kappa-conotoxin  
 CC PVIIA analogue of the invention.

XX  
 SQ Sequence 27 AA;

Query Match

Best Local Similarity 89.3%; Score 125; DB 22; Length 27;

Matches 21; Conservative 1; Mismatches 5; Indels 0; Gaps 0;



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AC AAU10207;
XX
XX 16-JAN-2002 (first entry)
XX
XX Snail Kappa-conotoxin PVIIA analogue R2Q.
DE
XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;
KM cardioactive; antisthmatic; KATP channel activation; cardiac ischaemia;
KM cerebral ischaemia; ocular ischaemia; asthma; R2Q.
XX
XX Conus purpurascens.
OS Synthetic.
XX
XX Key Location/Qualifiers
FH Modified-site 4
FT Modified-site /note="Hydroxyproline"
FT Modified-site 27
FT /note="The C-terminus is either a carboxyl group
FT or an amide group"
XX
XX WO200121648-A1.
XX
XX 29-MAR-2001.
XX
XX 21-SEP-2000; 2000WO-US25827.
XX
XX 22-SEP-1999; 99US-155135P.
XX 20-JUL-2000; 2000US-0219438.
XX
XX (COGN-) COGNETIX INC.
XX
XX Corneli-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;
XX Jones RR;
XX
XX WPI; 2001-648090/74.
XX
XX Treating disorders associated with radical depolarization of excitable
XX membrane e.g. cardiac, cerebral and ocular ischaemia and asthma
XX comprises activating a KATP channel by administering to an individual a
XX kappa-conotoxin PVIIA peptide -
XX
XX Claim 1; Page 28; 46pp; English.
XX
XX The invention relates to treating disorders associated with radical
XX depolarisation of excitable membrane by activating a KATP channel
XX comprising administering to an individual a kappa-conotoxin PVIIA
XX (kappa-PVIIA) peptide or its analogue, derivative or physiologically
XX active salt. The conotoxins are used for treating disorders associated
XX with radical depolarisation of excitable membrane by activating a KATP
XX channel, especially cardiac ischaemia, cerebral ischaemia, ocular
XX ischaemia and asthma. The present sequence is a kappa-conotoxin
XX PVIIA analogue of the invention.
XX
XX Sequence 27 AA;
XX
XX Query Match 88.6%; Score 124; DB 22; Length 27;
XX Best Local Similarity 77.8%; Pred. No. 2.1e-08;
XX Matches 21; Conservative 1; Mismatches 5; Indels 0; Gaps 0;
XX
XX QY 1 CRXNOKCFQHLDDCCSXCNXXNXC 27
XX I:||||| 11 11
XX 1 CRXNOKCFQHLDDCCSRKCNRFNKC 27
XX
XX RESULT 11
XX AAU10217
XX ID AAU10217 standard; peptide; 27 AA.
XX
XX AC AAU10217;
XX
XX 16-JAN-2002 (first entry)
XX
XX Snail Kappa-conotoxin PVIIA analogue V27A.
XX

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XX
XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;
KM cardioactive; antisthmatic; KATP channel activation; cardiac ischaemia;
KM cerebral ischaemia; ocular ischaemia; asthma; V27A.
XX
XX Conus purpurascens.
OS Synthetic.
XX
XX Key Location/Qualifiers
FH Modified-site 4
FT Modified-site /note="Hydroxyproline"
FT Modified-site 27
FT /note="The C-terminus is either a carboxyl group
FT or an amide group"
XX
XX WO200121648-A1.
XX
XX 29-MAR-2001.
XX
XX 21-SEP-2000; 2000WO-US25827.
XX
XX 22-SEP-1999; 99US-155135P.
XX 20-JUL-2000; 2000US-0219438.
XX
XX (COGN-) COGNETIX INC.
XX
XX Corneli-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;
XX Jones RR;
XX
XX WPI; 2001-648090/74.
XX
XX Treating disorders associated with radical depolarization of excitable
XX membrane e.g. cardiac, cerebral and ocular ischaemia and asthma
XX comprises activating a KATP channel by administering to an individual a
XX kappa-conotoxin PVIIA peptide -
XX
XX Claim 1; Page 28; 46pp; English.
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XX The invention relates to treating disorders associated with radical
XX depolarisation of excitable membrane by activating a KATP channel
XX comprising administering to an individual a kappa-conotoxin PVIIA
XX (kappa-PVIIA) peptide or its analogue, derivative or physiologically
XX active salt. The conotoxins are used for treating disorders associated
XX with radical depolarisation of excitable membrane by activating a KATP
XX channel, especially cardiac ischaemia, cerebral ischaemia, ocular
XX ischaemia and asthma. The present sequence is a kappa-conotoxin
XX PVIIA analogue of the invention.
XX
XX Sequence 27 AA;
XX
XX Query Match 88.6%; Score 124; DB 22; Length 27;
XX Best Local Similarity 80.8%; Pred. No. 2.1e-08;
XX Matches 21; Conservative 0; Mismatches 5; Indels 0; Gaps 0;
XX
XX QY 1 CRXNOKCFQHLDDCCSXCNXXNXC 26
XX I:||||| 11 11
XX 1 CRXNOKCFQHLDDCCSRKCNRFNKC 26
XX
XX RESULT 12
XX AAU10198
XX ID AAU10198 standard; peptide; 27 AA.
XX
XX AC AAU10198;
XX
XX 16-JAN-2002 (first entry)
XX
XX Snail Kappa-conotoxin PVIIA analogue I3A.
XX
XX Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory;
KM cardioactive; antisthmatic; KATP channel activation; cardiac ischaemia;
KM cerebral ischaemia; ocular ischaemia; asthma; I3A.
XX

```

OS Conus purpurascens.  
 OS Synthetic.  
 XX  
 FT Key  
 FT Modified-site 4 Location/Qualifiers  
 FT Modified-site 27 /note= "Hydroxyproline"  
 FT Modified-site 27 /note= "The C-terminus is either a carboxyl group or an amide group"  
 FT  
 XX  
 PN W0200121648-A1.  
 XX  
 XX  
 PD 29-MAR-2001.  
 XX  
 PF 21-SEP-2000; 2000WO-US25827.  
 XX  
 PR 22-SEP-1999; 99US-155135P.  
 PR 20-JUL-2000; 2000US-0219438.  
 XX  
 PA (COGN-) COGNETIX INC.  
 XX  
 PI Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
 PI Jones RR;  
 DR WPI: 2001-648090/74.  
 XX  
 XX Treating disorders associated with radical depolarization of excitable membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
 PT comprises activating a KATP channel by administering to an individual a kappa-conotoxin PVIIA peptide -  
 PT  
 PS Claim 1; Page 27; 46pp; English.  
 XX  
 CC The invention relates to treating disorders associated with radical depolarisation of excitable membrane by activating a KATP channel comprising administering to an individual a kappa-conotoxin PVIIA (kappa-PVIIA) peptide or its analogue, derivative or physiologically active salt. The conotoxins are used for treating disorders associated with radical depolarisation of excitable membrane by activating a KATP channel, especially cardiac ischemia, cerebral ischemia, ocular ischemia and asthma. The present sequence is a kappa-conotoxin CC PVIIA analogue of the invention.  
 CC  
 XX  
 SQ Sequence 27 AA;  
 Query Match 87.9%; Score 123; DB 22; Length 27;  
 Best Local Similarity 77.8%; Pred. No. 2.8e-08;  
 Matches 21; Conservative 0; Mismatches 6; Indels 0; Gaps 0;  
 QY 1 CRXNOKCFQHLDDCCSXCNXXNKCXV 27  
 DB 1 CRXNOKCFQHLDDCCSRKCNRFNKCXV 27  
 RESULT 13  
 AAU10214  
 ID AAU10214 standard; peptide; 27 AA.  
 XX  
 AC AAU10214;  
 XX  
 DT 16-JAN-2002 (first entry)  
 XX  
 DE Snail Kappa-conotoxin PVIIA analogue L12A.  
 XX  
 KW Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory; cardioactive; antilasthmatic; KATP channel activation; cardiac ischemia; cerebral ischemia; ocular ischemia; asthma; L12A.  
 KW  
 XX Conus purpurascens.  
 OS Synthetic.  
 OS  
 XX Key 4 Location/Qualifiers  
 FT Modified-site 4

FT Modified-site 27 /note= "Hydroxyproline"  
 FT Modified-site 27 /note= "The C-terminus is either a carboxyl group or an amide group"  
 FT  
 XX  
 PN W0200121648-A1.  
 XX  
 XX  
 PD 29-MAR-2001.  
 XX  
 PF 21-SEP-2000; 2000WO-US25827.  
 XX  
 PR 22-SEP-1999; 99US-155135P.  
 PR 20-JUL-2000; 2000US-0219438.  
 XX  
 PA (COGN-) COGNETIX INC.  
 XX  
 PI Cornell-Bell AH, Pemberton KE, Temple DL, Layer RT, McCabe RT;  
 PI Jones RR;  
 DR WPI: 2001-648090/74.  
 XX  
 XX Treating disorders associated with radical depolarization of excitable membrane e.g. cardiac, cerebral and ocular ischemia and asthma  
 PT comprises activating a KATP channel by administering to an individual a kappa-conotoxin PVIIA peptide -  
 PT  
 PS Claim 1; Page 28; 46pp; English.  
 XX  
 CC The invention relates to treating disorders associated with radical depolarisation of excitable membrane by activating a KATP channel comprising administering to an individual a kappa-conotoxin PVIIA (kappa-PVIIA) peptide or its analogue, derivative or physiologically active salt. The conotoxins are used for treating disorders associated with radical depolarisation of excitable membrane by activating a KATP channel, especially cardiac ischemia, cerebral ischemia, ocular ischemia and asthma. The present sequence is a kappa-conotoxin CC PVIIA analogue of the invention.  
 CC  
 XX  
 SQ Sequence 27 AA;  
 Query Match 87.9%; Score 123; DB 22; Length 27;  
 Best Local Similarity 77.8%; Pred. No. 2.8e-08;  
 Matches 21; Conservative 0; Mismatches 6; Indels 0; Gaps 0;  
 QY 1 CRXNOKCFQHLDDCCSXCNXXNKCXV 27  
 DB 1 CRXNOKCFQHLDDCCSRKCNRFNKCXV 27  
 RESULT 14  
 AAU10200  
 ID AAU10200 standard; peptide; 27 AA.  
 XX  
 AC AAU10200;  
 XX  
 DT 16-JAN-2002 (first entry)  
 XX  
 DE Snail Kappa-conotoxin PVIIA analogue R2A.  
 XX  
 KW Purple cone snail; kappa-conotoxin PVIIA analogue; circulatory; cardioactive; antilasthmatic; KATP channel activation; cardiac ischemia; cerebral ischemia; ocular ischemia; asthma; R2A.  
 KW  
 XX Conus purpurascens.  
 OS Synthetic.  
 OS  
 XX Key 4 Location/Qualifiers  
 FT Modified-site 4 /note= "Hydroxyproline"  
 FT Modified-site 27 /note= "The C-terminus is either a carboxyl group or an amide group"  
 FT



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## OM protein - protein search, using sw model

Run on: January 14, 2003, 18:27:36 ; Search time 14 Seconds  
(without alignments)  
56,744 Million cell updates/sec

Title: US-09-666-837B-1-COPY  
Perfect score: 140  
Sequence: 1 CRIKXNKCfQHDDCCSXKXNXXNKCXV 27

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 262574 seqs, 29422922 residues

Total number of hits satisfying chosen parameters: 262574

Minimum DB seq length: 0  
Maximum DB seq length: 200000000

Post-processing: Minimum Match 0%  
Maximum Match 100%  
Listing first 45 summaries

Database : Issued Patents AA:\*  
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2: /cgn2\_6/prodata/1/1aa/5B\_COMB.pep:\*  
3: /cgn2\_6/prodata/1/1aa/6A\_COMB.pep:\*  
4: /cgn2\_6/prodata/1/1aa/6B\_COMB.pep:\*  
5: /cgn2\_6/prodata/1/1aa/PCTUS\_COMB.pep:\*  
6: /cgn2\_6/prodata/1/1aa/Backfiles1.pep:\*

Pred. No. is the number of results predicted by chance to have a  
score greater than or equal to the score of the result being printed,  
and is derived by analysis of the total score distribution.

## SUMMARIES

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2	64	45.7	26	1	US-07-789-913-19
3	64	45.7	26	1	US-08-049-794-19
4	64	45.7	26	1	US-08-496-847-19
5	64	45.7	26	2	US-08-742-774-19
6	64	45.7	26	2	US-08-675-354-19
7	64	45.7	26	2	US-08-965-918-19
8	64	45.7	26	2	US-09-138-439-19
9	64	45.7	26	3	US-08-613-400A-19
10	64	45.7	26	3	US-09-298-017-19
11	64	45.7	26	4	US-09-392-979A-19
12	60	42.9	26	1	US-07-789-913-8
13	60	42.9	26	1	US-08-049-794-8
14	60	42.9	26	1	US-08-496-847-8
15	60	42.9	26	2	US-08-742-774-8
16	60	42.9	26	2	US-08-675-354-8
17	60	42.9	26	2	US-08-965-918-8
18	60	42.9	26	2	US-09-138-439-8
19	60	42.9	26	3	US-08-613-400A-8
20	60	42.9	26	3	US-09-298-017-8
21	60	42.9	26	4	US-09-392-979A-8
22	56	40.0	2523	1	US-08-185-432-18
23	56	40.0	2523	4	US-08-899-232-3
24	55	39.3	2703	4	US-08-185-432-19
25	55	39.3	2703	4	US-08-899-232-4
26	52	37.1	1964	4	US-09-467-997-1
27	52	37.1	2556	1	US-08-185-432-17

28	52	37.1	2556	1	US-08-083-550A-20	Sequence 20, Appl
29	52	37.1	2556	4	US-08-532-384-20	Sequence 20, Appl
30	52	37.1	2556	3	US-08-899-232-2	Sequence 2, Appl
31	50	35.7	26	1	US-08-049-794-21	Sequence 29, Appl
32	50	35.7	26	1	US-08-049-794-21	Sequence 29, Appl
33	50	35.7	26	1	US-08-496-847-21	Sequence 21, Appl
34	50	35.7	26	1	US-08-496-847-21	Sequence 21, Appl
35	50	35.7	26	2	US-08-742-774-21	Sequence 29, Appl
36	50	35.7	26	2	US-08-742-774-21	Sequence 29, Appl
37	50	35.7	26	2	US-08-675-354-21	Sequence 29, Appl
38	50	35.7	26	2	US-08-675-354-21	Sequence 29, Appl
39	50	35.7	26	2	US-08-965-918-21	Sequence 29, Appl
40	50	35.7	26	2	US-08-965-918-21	Sequence 29, Appl
41	50	35.7	26	2	US-09-138-439-21	Sequence 29, Appl
42	50	35.7	26	2	US-09-138-439-21	Sequence 29, Appl
43	50	35.7	26	3	US-08-613-400A-21	Sequence 21, Appl
44	50	35.7	26	3	US-08-613-400A-21	Sequence 29, Appl
45	50	35.7	26	3	US-09-298-017-21	Sequence 21, Appl

## ALIGNMENTS

RESULT 1  
US-08-619-936-1  
Sequence 1, Application US/08619936  
Patent No. 5672682  
GENERAL INFORMATION:  
APPLICANT: Terlau, Heinrich  
APPLICANT: Shon, Ki-Uoon  
APPLICANT: Grilley, Michelle  
APPLICANT: Oliveira, Baldomero M.  
TITLE OF INVENTION: Conotoxin Peptide PVIIA  
NUMBER OF SEQUENCES: 1  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Venable, Baetjer, Howard & Civiletti, LLP  
STREET: 1201 New York Avenue, Suite 1000  
CITY: Washington  
STATE: DC  
COUNTRY: U.S.A.  
ZIP: 20005  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: Patent Release #1.0, Version #1.30  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/619,936  
FILING DATE:  
CLASSIFICATION: 530  
ATTORNEY/AGENT INFORMATION:  
NAME: Saxe, Stephen A.  
REGISTRATION NUMBER: 38,609  
REFERENCE/DOCKET NUMBER: 24260-107674-04  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: 202-962-4848  
TELEFAX: 202-962-8300  
INFORMATION FOR SEQ ID NO: 1:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 27 amino acids  
TYPE: amino acid  
STRANDEDNESS: single  
TOPOLOGY: linear  
MOLECULE TYPE: peptide  
HYPOTHETICAL: NO  
ORIGINAL SOURCE:  
ORGANISM: Conus purpurascens  
FEATURE:  
NAME/KEY: Modified-site  
LOCATION: 4  
OTHER INFORMATION: /product="4Hyp"  
OTHER INFORMATION: /note="Amino acid 4 may be 4-trans-hydroxyproline."





GENERAL INFORMATION:  
APPLICANT: Amstutz, Gary A.  
APPLICANT: Bowersox, Stephen S.  
APPLICANT: Gohl, Kishorendra  
APPLICANT: Adriaenssens, Peter I.  
APPLICANT: Kristilpati, Ramasharma  
TITLE OF INVENTION: METHODS AND  
TITLE OF INVENTION: FORMULATIONS FOR PREVENTING PROGRESSION OF NEUROPATHIC PAIN  
NUMBER OF SEQUENCES: 36  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Dehlinger & Associates  
STREET: 350 Cambridge Avenue, Suite 250  
CITY: Palo Alto  
STATE: CA  
COUNTRY: US  
ZIP: 94306-1546  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Diskette  
COMPUTER: IBM compatible  
OPERATING SYSTEM: DOS  
SOFTWARE: Fastseo for Windows Version 2.0  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/496,847  
FILING DATE: 27-JUN-1995  
CLASSIFICATION: 514  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0009.31  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: 650-324-0880  
TELEFAX: 650-324-0960  
INFORMATION FOR SEQ ID NO: 19:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: amino acid  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHETICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-08-496-847-19

Query Match 45.7%; Score 64; DB 1; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.059;  
Matches 9; Conservative 4; Mismatches 13; Indels 0; Gaps 0;

OY 1 CRXNQCFOHLDCCSXCNXXNC 26  
DB 1 CKLKGSCSRIMWDCSCGSGRSGKC 26

RESULT 5  
US-08-742-774-19  
Sequence 19, Application US/08/42774  
Patent No. 5824645  
GENERAL INFORMATION:  
APPLICANT: JUSTICE, ALAN  
APPLICANT: SINGH, TEJINDER  
APPLICANT: GOHIL, KISHOR C  
APPLICANT: VALENTINO, KAREN L  
APPLICANT: MILJANICH, GEORGE P  
TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
TITLE OF INVENTION: ENHANCING OPIATE ANALGESIA  
NUMBER OF SEQUENCES: 34  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:

MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: Patentin Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/742,774  
FILING DATE:  
CLASSIFICATION:  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: 08/675,354  
FILING DATE: 03-JUL-1996  
APPLICATION NUMBER: US/08/049,794  
FILING DATE: 1993-APR-15  
APPLICATION NUMBER: US/07/814,759  
FILING DATE: 30-DEC-1991  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0009.30  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: (415) 324-0880  
TELEFAX: (415) 324-0960  
INFORMATION FOR SEQ ID NO: 19:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: amino acid  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHETICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-08-742-774-19

Query Match 45.7%; Score 64; DB 2; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.059;  
Matches 9; Conservative 4; Mismatches 13; Indels 0; Gaps 0;

OY 1 CRXNQCFOHLDCCSXCNXXNC 26  
DB 1 CKLKGSCSRIMWDCSCGSGRSGKC 26

RESULT 6  
US-08-675-354-19  
Sequence 19, Application US/08/675354  
Patent No. 5859186  
GENERAL INFORMATION:  
APPLICANT: JUSTICE, ALAN  
APPLICANT: SINGH, TEJINDER  
APPLICANT: GOHIL, KISHOR C  
APPLICANT: VALENTINO, KAREN L  
APPLICANT: MILJANICH, GEORGE P  
TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
TITLE OF INVENTION: ENHANCING OPIATE ANALGESIA  
NUMBER OF SEQUENCES: 34  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: Patentin Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/675,354  
FILING DATE: 03-JUL-1996  
CLASSIFICATION: 530  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: US/08/049,794

;  
HYPOTHETICAL: NO

[illegible]

```
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Db 1 CKLKGQSCSRMLMYDCCSGSCGRSGKC 26
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RESULT 9  
US-08-613-400A-19  
Sequence 19, Application US/08613400A  
Patent No. 6054429  
GENERAL INFORMATION:  
APPLICANT: Bowersox, S. Scott  
APPLICANT: Gadbois, Theresa  
APPLICANT: Pettus, Mark, R.  
APPLICANT: Luther, Robert, R.  
TITLE OF INVENTION: IMPROVED EPIDURAL  
TITLE OF INVENTION: METHOD OF PRODUCING ANALGESIA  
NUMBER OF SEQUENCES: 36  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Dehlinger & Associates  
STREET: 350 Cambridge Avenue, Suite 250  
CITY: Palo Alto  
STATE: CA  
COUNTRY: US  
ZIP: 94306-1546  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Diskette  
COMPUTER: IBM Compatible  
OPERATING SYSTEM: DOS  
SOFTWARE: FastSeq for Windows Version 2.0  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/613,400A  
FILING DATE: 08-MAR-1996  
CLASSIFICATION: 514  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER:  
FILING DATE:  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0019  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: 650-324-0880  
TELEFAX: 650-324-0960  
INFORMATION FOR SEQ ID NO: 19:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: amino acid  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHEICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-08-613-400A-19  
Query Match 45.7%; Score 64; DB 3; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.059;  
Matches 9; Conservative 4; Mismatches 13; Indels 0; Gaps 0;  
OY 1 CRXNKCFOHLDCCSXCNXXNC 26  
DB 1 CKLKGSCSRIMYDCSGSGRSGKC 26  
RESULT 10  
US-09-298-017-19  
Sequence 19, Application US/09298017  
Patent No. 6087091  
GENERAL INFORMATION:  
APPLICANT: JUSTICE, ALAN  
APPLICANT: SINGH, TEJINDER  
APPLICANT: GOHIL, KISHOR C  
APPLICANT: VALENTINO, KAREN L  
APPLICANT: MILVANICH, GEORGE P  
TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
TITLE OF INVENTION: ENHANCING OPiate ANALGESIA  
NUMBER OF SEQUENCES: 34  
CORRESPONDENCE ADDRESS:

ADDRESSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: PatentIn Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/09/298,017  
FILING DATE:  
CLASSIFICATION:  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: 08/049,794  
FILING DATE:  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0009.30  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: (415) 324-0880  
TELEFAX: (415) 324-0960  
INFORMATION FOR SEQ ID NO: 19:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: amino acid  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHEICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-09-298-017-19  
Query Match 45.7%; Score 64; DB 3; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.059;  
Matches 9; Conservative 4; Mismatches 13; Indels 0; Gaps 0;  
OY 1 CRXNKCFOHLDCCSXCNXXNC 26  
DB 1 CKLKGSCSRIMYDCSGSGRSGKC 26  
RESULT 11  
US-09-392-979A-19  
Sequence 19, Application US/09392979A  
Patent No. 6136786  
GENERAL INFORMATION:  
APPLICANT: JUSTICE, ALAN  
APPLICANT: SINGH, TEJINDER  
APPLICANT: GOHIL, KISHOR C  
APPLICANT: VALENTINO, KAREN L  
APPLICANT: MILVANICH, GEORGE P  
TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
TITLE OF INVENTION: ENHANCING OPiate ANALGESIA  
NUMBER OF SEQUENCES: 34  
CORRESPONDENCE ADDRESS:  
ADDRESSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: PatentIn Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/09/392,979A  
FILING DATE:

CLASSIFICATION:  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: US/08/049,794  
FILING DATE: 1993-04-15  
APPLICATION NUMBER: US 07/814,759  
FILING DATE: 30-DEC-1991  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0009.30  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: (415) 324-0880  
TELEFAX: (415) 324-0960  
INFORMATION FOR SEQ ID NO: 19:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: amino acid  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHETICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-202, FIGURE 2  
US-09-392-979A-19

Query Match 45.7%; Score 64; DB 4; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.059;  
Matches 9; Conservative 4; Mismatches 13; Indels 0; Gaps 0;  
QY 1 CRXNKCQFQHLDDCCSXCNXNC 26  
DB 1 CKLKGSCRLMYDCCSGSGCRSGKC 26

RESULT 12  
US-07-789-913-8  
Sequence 8, Application US/07789913  
Patent No. 5559095  
GENERAL INFORMATION:  
APPLICANT: Miljanich, George P.  
APPLICANT: Bowersox, Stephen S.  
APPLICANT: Fox, James A.  
APPLICANT: Valentino, Karen L.  
APPLICANT: Bilter, Robert S.  
APPLICANT: Yamashiro, Donald H.  
TITLE OF INVENTION: Delayed Treatment Method of Reducing  
TITLE OF INVENTION: Ischemia-Related Neuronal Damage  
NUMBER OF SEQUENCES: 28  
CORRESPONDENCE ADDRESSES:  
ADDRESSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: Patentin Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/07/789,913  
FILING DATE: 19911112  
CLASSIFICATION: 514  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: US 07/561,766  
FILING DATE: 02-AUG-1990  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: US 07/440,094  
FILING DATE: 22-NOV-1989  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0005.30

TELECOMMUNICATION INFORMATION:  
TELEPHONE: (415) 324-0880  
TELEFAX: (415) 324-0960  
INFORMATION FOR SEQ ID NO: 8:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: AMINO ACID  
TOPOLOGY: both  
MOLECULE TYPE: peptide  
HYPOTHETICAL: NO  
ANTI-SENSE: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SNX-183  
US-07-789-913-8

Query Match 42.9%; Score 60; DB 1; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.18;  
Matches 9; Conservative 3; Mismatches 14; Indels 0; Gaps 0;  
QY 1 CRXNKCQFQHLDDCCSXCNXNC 26  
DB 1 CKLKGSCRLMYDCCSGSGCRSGKC 26

RESULT 13  
US-08-049-794-8  
Sequence 8, Application US/08049794  
Patent No. 5587454  
GENERAL INFORMATION:  
APPLICANT: JUSTICE, ALAN  
APPLICANT: SINGH, TEJINDER  
APPLICANT: GOHIL, KISHOR C  
APPLICANT: VALENTINO, KAREN L.  
APPLICANT: MILJANICH, GEORGE P.  
TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
TITLE OF INVENTION: ENHANCING OPIATE ANALGESIA  
NUMBER OF SEQUENCES: 34  
CORRESPONDENCE ADDRESSES:  
ADDRESSEE: Law Offices of Peter Dehlinger  
STREET: 350 Cambridge Avenue, Suite 300  
CITY: Palo Alto  
STATE: CA  
COUNTRY: USA  
ZIP: 94306  
COMPUTER READABLE FORM:  
MEDIUM TYPE: Floppy disk  
COMPUTER: IBM PC compatible  
OPERATING SYSTEM: PC-DOS/MS-DOS  
SOFTWARE: Patentin Release #1.0, Version #1.25  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/08/049,794  
FILING DATE: 19930415  
CLASSIFICATION: 514  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER: US 07/814,759  
FILING DATE: 30-DEC-1991  
ATTORNEY/AGENT INFORMATION:  
NAME: Stratford, Carol A.  
REGISTRATION NUMBER: 34,444  
REFERENCE/DOCKET NUMBER: 5865-0009.30  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: (415) 324-0880  
TELEFAX: (415) 324-0960  
INFORMATION FOR SEQ ID NO: 8:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 26 amino acids  
TYPE: AMINO ACID  
TOPOLOGY: linear  
MOLECULE TYPE: protein  
HYPOTHETICAL: NO  
ORIGINAL SOURCE:  
INDIVIDUAL ISOLATE: SV1B/SNX-183, FIGURE 1  
US-08-049-794-8

Query Match 42.9%; Score 60; DB 1; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.18;  
Matches 9; Conservative 3; Mismatches 14; Indels 0; Gaps 0;

QY 1 CRXNOKCFQHLDDCCSXKCNXXNC 26  
|::|::|::|::|::|::|  
Db 1 CKLKGSCRTSYDCSGSGRSGKC 26

RESULT 14  
US-08-496-847-8

; Sequence 8, Application US/08496847  
; Patent No. 5795864  
; GENERAL INFORMATION:  
; APPLICANT: Amstutz, Gary A.  
; APPLICANT: Bowersox, Stephen S.  
; APPLICANT: Gohli, Kishorchandra  
; APPLICANT: Adriaenssens, Peter I.  
; APPLICANT: Kristipati, Ramasharma  
; TITLE OF INVENTION: METHODS AND  
; TITLE OF INVENTION: FORMULATIONS FOR PREVENTING PROGRESSION OF NEUROPATHIC PAIN  
; NUMBER OF SEQUENCES: 36  
; CORRESPONDENCE ADDRESS:  
; ADDRESSEE: Dehlinger & Associates  
; STREET: 350 Cambridge Avenue, Suite 250  
; CITY: Palo Alto  
; STATE: CA  
; COUNTRY: US  
; ZIP: 94306-1546  
; COMPUTER READABLE FORM:  
; MEDIUM TYPE: Diskette  
; COMPUTER: IBM Compatible  
; OPERATING SYSTEM: DOS  
; SOFTWARE: FastSeq for Windows Version 2.0  
; CURRENT APPLICATION DATA:  
; APPLICATION NUMBER: US/08/496,847  
; FILING DATE: 27-JUN-1995  
; CLASSIFICATION: 514  
; ATTORNEY/AGENT INFORMATION:  
; NAME: Stratford, Carol A  
; REGISTRATION NUMBER: 34,444  
; REFERENCE/DOCKET NUMBER: 5865-0009.31  
; TELECOMMUNICATION INFORMATION:  
; TELEPHONE: 650-324-0880  
; TELEFAX: 650-324-0960  
; INFORMATION FOR SEQ ID NO: 8:  
; SEQUENCE CHARACTERISTICS:  
; LENGTH: 26 amino acids  
; TYPE: amino acid  
; TOPOLOGY: linear  
; MOLECULE TYPE: protein  
; HYPOTHETICAL: NO  
; ORIGINAL SOURCE:  
; INDIVIDUAL ISOLATE: SVIB/SNX-183, FIGURE 1  
; US-08-496-847-8

Query Match 42.9%; Score 60; DB 1; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.18;  
Matches 9; Conservative 3; Mismatches 14; Indels 0; Gaps 0;

QY 1 CRXNOKCFQHLDDCCSXKCNXXNC 26  
|::|::|::|::|::|::|  
Db 1 CKLKGSCRTSYDCSGSGRSGKC 26

RESULT 15  
US-08-742-774-8  
; Sequence 8, Application US/08742774  
; Patent No. 5824645  
; GENERAL INFORMATION:  
; APPLICANT: JUSTICE, ALAN  
; APPLICANT: SINGH, TEJINDER

; APPLICANT: GOHLI, KISHOR C  
; APPLICANT: VALENTINO, KAREN L  
; APPLICANT: MILJANICH, GEORGE P  
; TITLE OF INVENTION: METHODS OF PRODUCING ANALGESIA AND  
; TITLE OF INVENTION: ENHANCING OPIATE ANALGESIA  
; NUMBER OF SEQUENCES: 34  
; CORRESPONDENCE ADDRESS:  
; ADDRESSEE: Law Offices of Peter Dehlinger  
; STREET: 350 Cambridge Avenue, Suite 300  
; CITY: Palo Alto  
; STATE: CA  
; COUNTRY: USA  
; ZIP: 94306

; COMPUTER READABLE FORM:  
; MEDIUM TYPE: Floppy disk  
; COMPUTER: IBM PC compatible  
; OPERATING SYSTEM: PC-DOS/MS-DOS  
; SOFTWARE: PatentIn Release #1.0, Version #1.25  
; CURRENT APPLICATION DATA:  
; APPLICATION NUMBER: US/08/742,774  
; FILING DATE:  
; CLASSIFICATION:  
; PRIOR APPLICATION DATA:  
; APPLICATION NUMBER: 08/675,354  
; FILING DATE: 03-JUL-1996  
; APPLICATION NUMBER: US/08/049,794  
; FILING DATE: 1993-APR-15  
; APPLICATION NUMBER: US 07/814,759  
; FILING DATE: 30-DEC-1991  
; ATTORNEY/AGENT INFORMATION:  
; NAME: Stratford, Carol A.  
; REGISTRATION NUMBER: 34,444  
; REFERENCE/DOCKET NUMBER: 5865-0009.30  
; TELECOMMUNICATION INFORMATION:  
; TELEPHONE: (415) 324-0880  
; TELEFAX: (415) 324-0960  
; INFORMATION FOR SEQ ID NO: 8:  
; SEQUENCE CHARACTERISTICS:  
; LENGTH: 26 amino acids  
; TYPE: amino acid  
; TOPOLOGY: linear  
; MOLECULE TYPE: protein  
; HYPOTHETICAL: NO  
; ORIGINAL SOURCE:  
; INDIVIDUAL ISOLATE: SVIB/SNX-183, FIGURE 1  
; US-08-742-774-8

Query Match 42.9%; Score 60; DB 2; Length 26;  
Best Local Similarity 34.6%; Pred. No. 0.18;  
Matches 9; Conservative 3; Mismatches 14; Indels 0; Gaps 0;

QY 1 CRXNOKCFQHLDDCCSXKCNXXNC 26  
|::|::|::|::|::|::|  
Db 1 CKLKGSCRTSYDCSGSGRSGKC 26

Search completed: January 14, 2003, 18:29:47  
Job time : 15 secs



GenCore version 5.1.3  
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OM protein - protein search, using sw model

Run on: January 14, 2003, 18:28:16 ; Search time 11 Seconds  
(without alignments)  
47.621 Million cell updates/sec

Title: US-09-666-837b-1-COPY  
Perfect score: 140  
Sequence: 1 CRXNCKCFDHDCCSXNXXNXCXV 27

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 118974 seqs, 19401057 residues

Total number of hits satisfying chosen parameters: 118974

Minimum DB seq length: 0  
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%  
Maximum Match 100%

Listing first 45 summaries

Database : Published Applications-AA:\*

- 1: /cgn2\_6/ptodata/2/pubppaa/US08\_NEW\_PUB.pep.\*
- 2: /cgn2\_6/ptodata/2/pubppaa/PCY\_NEW\_PUB.pep.\*
- 3: /cgn2\_6/ptodata/2/pubppaa/US06\_NEW\_PUB.pep.\*
- 4: /cgn2\_6/ptodata/2/pubppaa/US06\_PUBCOMB.pep.\*
- 5: /cgn2\_6/ptodata/2/pubppaa/US07\_NEW\_PUB.pep.\*
- 6: /cgn2\_6/ptodata/2/pubppaa/US07\_PUBCOMB.pep.\*
- 7: /cgn2\_6/ptodata/2/pubppaa/PCYUS\_PUBCOMB.pep.\*
- 8: /cgn2\_6/ptodata/2/pubppaa/US08\_PUBCOMB.pep.\*
- 9: /cgn2\_6/ptodata/2/pubppaa/US09\_NEW\_PUB.pep.\*
- 10: /cgn2\_6/ptodata/2/pubppaa/US09\_PUBCOMB.pep.\*
- 11: /cgn2\_6/ptodata/2/pubppaa/US10\_NEW\_PUB.pep.\*
- 12: /cgn2\_6/ptodata/2/pubppaa/US10\_PUBCOMB.pep.\*
- 13: /cgn2\_6/ptodata/2/pubppaa/US60\_NEW\_PUB.pep.\*
- 14: /cgn2\_6/ptodata/2/pubppaa/US60\_PUBCOMB.pep.\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	% Match	Query Length	ID	Description
1	58.5	41.8	35	10	US-09-894-882-120
2	56.5	40.4	35	10	US-09-894-882-413
3	56.5	40.4	36	10	US-09-894-882-168
4	56.5	40.4	36	10	US-09-894-882-210
5	56.5	40.4	36	10	US-09-894-882-404
6	56.5	40.4	70	10	US-09-894-882-209
7	56.5	40.4	71	10	US-09-894-882-119
8	55.5	39.6	36	10	US-09-894-882-201
9	55.5	39.6	36	10	US-09-894-882-401
10	55.5	39.6	42	10	US-09-894-882-306
11	55.5	39.6	42	10	US-09-894-882-452
12	55.5	39.6	70	10	US-09-894-882-200
13	55.5	39.6	75	10	US-09-894-882-305
14	54.5	38.9	36	10	US-09-894-882-369
15	54.5	38.9	73	10	US-09-894-882-167
16	52.5	37.1	35	10	US-09-894-882-75
17	52	37.1	2444	10	US-09-944-849-2
18	51.5	36.8	35	10	US-09-894-882-159
19	51.5	36.8	36	10	US-09-894-882-156

20	51.5	36.8	36	10	US-09-894-882-174	Sequence 174, App
21	51.5	36.8	36	10	US-09-894-882-177	Sequence 177, App
22	51.5	36.8	36	10	US-09-894-882-403	Sequence 403, App
23	51.5	36.8	37	10	US-09-894-882-426	Sequence 426, App
24	51.5	36.8	70	10	US-09-894-882-206	Sequence 206, App
25	50.5	36.1	35	10	US-09-894-882-433	Sequence 433, App
26	50.5	36.1	36	10	US-09-894-882-216	Sequence 216, App
27	50.5	36.1	36	10	US-09-894-882-406	Sequence 406, App
28	50.5	36.1	42	10	US-09-894-882-309	Sequence 309, App
29	50.5	36.1	42	10	US-09-894-882-312	Sequence 312, App
30	50.5	36.1	42	10	US-09-894-882-449	Sequence 449, App
31	50.5	36.1	42	10	US-09-894-882-450	Sequence 450, App
32	50.5	36.1	70	10	US-09-894-882-215	Sequence 215, App
33	50.5	36.1	71	10	US-09-894-882-74	Sequence 74, App
34	50.5	36.1	75	10	US-09-894-882-308	Sequence 308, App
35	50.5	36.1	75	10	US-09-894-882-311	Sequence 311, App
36	50.5	36.1	76	9	US-09-749-599-4	Sequence 4, App
37	50	35.7	176	9	US-10-024-599-4	Sequence 208, App
38	49.5	35.4	29	9	US-09-749-637A-208	Sequence 366, App
39	49.5	35.4	35	10	US-09-894-882-366	Sequence 165, App
40	49.5	35.4	36	10	US-09-894-882-165	Sequence 207, App
41	49.5	35.4	36	10	US-09-894-882-207	Sequence 365, App
42	49.5	35.4	36	10	US-09-894-882-365	Sequence 368, App
43	49.5	35.4	36	10	US-09-894-882-368	Sequence 371, App
44	49.5	35.4	36	10	US-09-894-882-371	Sequence 372, App
45	49.5	35.4	36	10	US-09-894-882-372	

## ALIGNMENTS

RESULT 1  
US-09-894-882-120  
; Sequence 120, Application US/09894882  
; Patent No. US20020102607A1  
; GENERAL INFORMATION:  
; APPLICANT: University of Utah Research Foundation  
; APPLICANT: Cognetix, Inc.  
; APPLICANT: Walker, Craig S.  
; APPLICANT: Shetty, Reshma  
; APPLICANT: Jimenez, Elsie C.  
; APPLICANT: McIntosh, J. Michael  
; APPLICANT: Olivera, Baldemero M.  
; APPLICANT: Watkins, Maren  
; APPLICANT: Jones, Robert M.  
; APPLICANT: Shen, Greg S.  
; TITLE OF INVENTION: I-Superfamily Conotoxins  
; FILE REFERENCE: 2314-238  
; CURRENT APPLICATION NUMBER: US/09/894, 882  
; PRIOR FILING DATE: 2001-06-29  
; PRIOR APPLICATION NUMBER: US 60/  
; PRIOR FILING DATE: 2000-06-30  
; PRIOR APPLICATION NUMBER: US 60/243,410  
; PRIOR FILING DATE: 2000-10-27  
; PRIOR APPLICATION NUMBER: US 60/246,581  
; PRIOR FILING DATE: 2000-11-08  
; PRIOR APPLICATION NUMBER: US 60/247,714  
; PRIOR FILING DATE: 2000-11-14  
; PRIOR APPLICATION NUMBER: US 60/264,256  
; PRIOR FILING DATE: 2001-01-29  
; NUMBER OF SEQ ID NOS: 506  
; SOFTWARE: PatentIn version 3.0  
; SEQ ID NO 120  
; LENGTH: 35  
; TYPE: PRT  
; ORGANISM: Conus magus  
; FEATURE:  
; NAME/KEY: PEPTIDE  
; LOCATION: (1)..(35)  
; OTHER INFORMATION: Xaa at residue 33 is Pro or hydroxy-Pro; Xaa at residue 25 is  
; OTHER INFORMATION: or gamma-carboxy-Glu; Xaa at residue 18 is Trp or bromo-Tr  
US-09-894-882-120





OTHER INFORMATION: Tyr, 125I-Tyr, mono-Iodo-Tyr, di-Iodo-Tyr, O-sulpho-Tyr or O-pho  
; OTHER INFORMATION: spho-Tyr  
US-09-894-882-210

Query Match 40.4%; Score 56.5; DB 10; Length 36;  
Best Local Similarity 44.4%; Pred. No. 0.14;  
Matches 12; Conservative 1; Mismatches 13; Indels 1; Gaps 1;

OY 1 CRXNOKCFQHLDDCSXXCNXXNXC 27  
|| | |||: | | | |  
Db 5 CFNAGVKCDNH-SDCCADTCCYDNTCV 30

RESULT 5  
US-09-894-882-404  
; Sequence 404; Application US/09894882  
; Patent No. US20020102607A1

GENERAL INFORMATION:

APPLICANT: University of Utah Research Foundation

APPLICANT: Cognetix, Inc.

APPLICANT: Walker, Craig S.

APPLICANT: Shetty, Reshma

APPLICANT: Jimenez, Elsie C.

APPLICANT: McIntosh, J. Michael

APPLICANT: Olivera, Baldomero M.

APPLICANT: Watkins, Maren

APPLICANT: Jones, Robert M.

APPLICANT: Shen, Greg S.

TITLE OF INVENTION: I-Superfamily Conotoxins

FILE REFERENCE: 2314-238

CURRENT APPLICATION NUMBER: US/09/894,882

CURRENT FILING DATE: 2001-06-29

PRIOR APPLICATION NUMBER: US 60/

PRIOR FILING DATE: 2000-06-30

PRIOR APPLICATION NUMBER: US 60/243,410

PRIOR FILING DATE: 2000-10-27

PRIOR APPLICATION NUMBER: US 60/246,581

PRIOR FILING DATE: 2000-11-08

PRIOR APPLICATION NUMBER: US 60/247,714

PRIOR FILING DATE: 2000-11-14

PRIOR APPLICATION NUMBER: US 60/264,256

PRIOR FILING DATE: 2001-01-29

NUMBER OF SEQ ID NOS: 506

SOFTWARE: PatentIn version 3.0

SEQ ID NO 404

LENGTH: 36

TYPE: PRT

ORGANISM: Conus lynceus

US-09-894-882-404

Query Match 40.4%; Score 56.5; DB 10; Length 36;  
Best Local Similarity 40.7%; Pred. No. 0.14;  
Matches 11; Conservative 1; Mismatches 14; Indels 1; Gaps 1;

OY 1 CRXNOKCFQHLDDCSXXCNXXNXC 27  
|| | |||: | | | |  
Db 5 CFNAGVKCDNH-SDCCADTCCYDNTCV 30

RESULT 6  
US-09-894-882-209  
; Sequence 209; Application US/09894882  
; Patent No. US20020102607A1

GENERAL INFORMATION:

APPLICANT: University of Utah Research Foundation

APPLICANT: Cognetix, Inc.

APPLICANT: Walker, Craig S.

APPLICANT: Shetty, Reshma

APPLICANT: Jimenez, Elsie C.

APPLICANT: McIntosh, J. Michael

APPLICANT: Olivera, Baldomero M.

APPLICANT: Watkins, Maren

APPLICANT: Jones, Robert M.

APPLICANT: Shen, Greg S.

TITLE OF INVENTION: I-Superfamily Conotoxins

FILE REFERENCE: 2314-238

CURRENT APPLICATION NUMBER: US/09/894,882

CURRENT FILING DATE: 2001-06-29

PRIOR APPLICATION NUMBER: US 60/

PRIOR FILING DATE: 2000-06-30

PRIOR APPLICATION NUMBER: US 60/243,410

PRIOR FILING DATE: 2000-10-27

PRIOR APPLICATION NUMBER: US 60/246,581

PRIOR FILING DATE: 2000-11-08

PRIOR APPLICATION NUMBER: US 60/247,714

PRIOR FILING DATE: 2000-11-14

PRIOR APPLICATION NUMBER: US 60/264,256

PRIOR FILING DATE: 2001-01-29

NUMBER OF SEQ ID NOS: 506

SOFTWARE: PatentIn version 3.0

SEQ ID NO 209

LENGTH: 70

TYPE: PRT

ORGANISM: Conus lynceus

US-09-894-882-209

Query Match 40.4%; Score 56.5; DB 10; Length 70;  
Best Local Similarity 40.7%; Pred. No. 0.26;  
Matches 11; Conservative 1; Mismatches 14; Indels 1; Gaps 1;

OY 1 CRXNOKCFQHLDDCSXXCNXXNXC 27  
|| | |||: | | | |  
Db 39 CFNAGVKCDNH-SDCCADTCCYDNTCV 64

RESULT 7  
US-09-894-882-119  
; Sequence 119; Application US/09894882  
; Patent No. US20020102607A1

GENERAL INFORMATION:

APPLICANT: University of Utah Research Foundation

APPLICANT: Cognetix, Inc.

APPLICANT: Walker, Craig S.

APPLICANT: Shetty, Reshma

APPLICANT: Jimenez, Elsie C.

APPLICANT: McIntosh, J. Michael

APPLICANT: Olivera, Baldomero M.

APPLICANT: Watkins, Maren

APPLICANT: Jones, Robert M.

APPLICANT: Shen, Greg S.

TITLE OF INVENTION: I-Superfamily Conotoxins

FILE REFERENCE: 2314-238

CURRENT APPLICATION NUMBER: US/09/894,882

CURRENT FILING DATE: 2001-06-29

PRIOR APPLICATION NUMBER: US 60/

PRIOR FILING DATE: 2000-06-30

PRIOR APPLICATION NUMBER: US 60/243,410

PRIOR FILING DATE: 2000-10-27

PRIOR APPLICATION NUMBER: US 60/246,581

PRIOR FILING DATE: 2000-11-08

PRIOR APPLICATION NUMBER: US 60/247,714

PRIOR FILING DATE: 2000-11-14

PRIOR APPLICATION NUMBER: US 60/264,256

PRIOR FILING DATE: 2001-01-29

NUMBER OF SEQ ID NOS: 506

SOFTWARE: PatentIn version 3.0

SEQ ID NO 119

LENGTH: 71

TYPE: PRT

ORGANISM: Conus magus

US-09-894-882-119

Query Match 40.4%; Score 56.5; DB 10; Length 71;  
Best Local Similarity 37.0%; Pred. No. 0.26;  
Matches 10; Conservative 2; Mismatches 14; Indels 1; Gaps 1;

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? FILE REFERENCE: 2314-238
? CURRENT APPLICATION NUMBER: US/09/894,882
? CURRENT FILING DATE: 2001-06-29
? PRIOR APPLICATION NUMBER: US 60/
? PRIOR FILING DATE: 2000-06-30
? PRIOR APPLICATION NUMBER: US 60/243,410
? PRIOR FILING DATE: 2000-10-27
? PRIOR APPLICATION NUMBER: US 60/246,581
? PRIOR FILING DATE: 2000-11-08
? PRIOR APPLICATION NUMBER: US 60/247,714
? PRIOR FILING DATE: 2000-11-14
? PRIOR APPLICATION NUMBER: US 60/264,256
? PRIOR FILING DATE: 2001-01-29
? NUMBER OF SEQ ID NOS: 506
? SOFTWARE: PatentIn version 3.0
? SEQ ID NO 401
? LENGTH: 36
? TYPE: PRT
? ORGANISM: Conus lynceus
US-09-894-882-401

Query Match          39.6%; Score 55.5; DB 10; Length 36;
Best Local Similarity 40.7%; Pred. No. 0.2;
Matches 11; Conservative 0; Mismatches 15; Indels 1; Gaps 1;

OY      1 CRINXNCKCFQHLDDCCSXKXCNXKCV 27
        |  |  |  |  |  |  |  |  |  |  |
DB      5 CFNAGYKCDNH-SDCCEDTCYDNTCV 30

RESULT 10
US-09-894-882-306
? Sequence 306, Application US/09894882
? Patent No. US20020102607A1
? GENERAL INFORMATION:
? APPLICANT: University of Utah Research Foundation
? APPLICANT: Cognetix, Inc.
? APPLICANT: Walker, Craig S.
? APPLICANT: Shetty, Reshma
? APPLICANT: Jimenez, Elsie C.
? APPLICANT: McIntosh, J. Michael
? APPLICANT: Olivera, Baldomero M.
? APPLICANT: Watkins, Maeha
? APPLICANT: Jones, Robert M.
? APPLICANT: Shen, Greg S.
? TITLE OF INVENTION: I-Superfamily Conotoxins
? FILE REFERENCE: 2314-238
? CURRENT APPLICATION NUMBER: US/09/894,882
? CURRENT FILING DATE: 2001-06-29
? PRIOR APPLICATION NUMBER: US 60/
? PRIOR FILING DATE: 2000-06-30
? PRIOR APPLICATION NUMBER: US 60/243,410
? PRIOR FILING DATE: 2000-10-27
? PRIOR APPLICATION NUMBER: US 60/246,581
? PRIOR FILING DATE: 2000-11-08
? PRIOR APPLICATION NUMBER: US 60/247,714
? PRIOR FILING DATE: 2000-11-14
? PRIOR APPLICATION NUMBER: US 60/264,256
? PRIOR FILING DATE: 2001-01-29
? NUMBER OF SEQ ID NOS: 506
? SOFTWARE: PatentIn version 3.0
? SEQ ID NO 306
? LENGTH: 42
? TYPE: PRT
? ORGANISM: Conus aulicus
? FEATURE:
? NAME/KEY: PEPTIDE
? LOCATION: (1)..(42)
? OTHER INFORMATION: Xaa at residue 36 is pro or hydroxy-Pro; Xaa at residue 12 is
? OTHER INFORMATION: or gamma-carboxy-Glu; Xaa at residues 3 and 8 is Trp or bromo-
? OTHER INFORMATION: P; Xaa at residue 34 is Tyr, 125i-Tyr, mono-Iodo-Tyr, di-Iodo-
? OTHER INFORMATION: , O-sulpho-Tyr or O-phospho-Tyr
US-09-894-882-306

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Query Match          39.6%; Score 55.5; DB 10; Length 42;
Best Local Similarity 33.3%; Pred. No. 0.22;
Matches 9; Conservative 3; Mismatches 14; Indels 1; Gaps 1;

OY 1 CRXNOKCFQHLDDCCSXKCNXXNXCVCV 27
DB 6 CSMSGQEC-KHVSDDCGSFCCVGRCL 31

RESULT 11
US-09-894-882-452
; Sequence 452, Application US/09894882
; Patent No. US20020102607A1
; GENERAL INFORMATION:
; APPLICANT: University of Utah Research Foundation
; APPLICANT: Cognetix, Inc.
; APPLICANT: Walker, Craig S.
; APPLICANT: Shetty, Reshma
; APPLICANT: Jimenez, Elsie C.
; APPLICANT: McIntosh, J. Michael
; APPLICANT: Olivera, Baldomero M.
; APPLICANT: Watkins, Maren
; APPLICANT: Jones, Robert M.
; APPLICANT: Shen, Greg S.
; TITLE OF INVENTION: I-Superfamily Conotoxins
; FILE REFERENCE: 2314-238
; CURRENT APPLICATION NUMBER: US/09/894, 882
; PRIOR FILING DATE: 2001-06-29
; PRIOR APPLICATION NUMBER: US 60/
; PRIOR FILING DATE: 2000-06-30
; PRIOR APPLICATION NUMBER: US 60/243,410
; PRIOR FILING DATE: 2000-10-27
; PRIOR APPLICATION NUMBER: US 60/246,581
; PRIOR FILING DATE: 2000-11-08
; PRIOR APPLICATION NUMBER: US 60/247,714
; PRIOR FILING DATE: 2000-11-14
; PRIOR APPLICATION NUMBER: US 60/264,256
; PRIOR FILING DATE: 2001-01-29
; NUMBER OF SEQ ID NOS: 506
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 452
; LENGTH: 42
; TYPE: PRT
; ORGANISM: Conus aulicus
US-09-894-882-452

Query Match          39.6%; Score 55.5; DB 10; Length 42;
Best Local Similarity 33.3%; Pred. No. 0.22;
Matches 9; Conservative 4; Mismatches 13; Indels 1; Gaps 1;

OY 1 CRXNOKCFQHLDDCCSXKCNXXNXCVCV 27
DB 6 CSMSGQEC-KHVSDDCGSFCCVGRCL 31

RESULT 12
US-09-894-882-200
; Sequence 200, Application US/09894882
; Patent No. US20020102607A1
; GENERAL INFORMATION:
; APPLICANT: University of Utah Research Foundation
; APPLICANT: Cognetix, Inc.
; APPLICANT: Walker, Craig S.
; APPLICANT: Shetty, Reshma
; APPLICANT: Jimenez, Elsie C.
; APPLICANT: McIntosh, J. Michael
; APPLICANT: Olivera, Baldomero M.
; APPLICANT: Watkins, Maren
; APPLICANT: Jones, Robert M.
; APPLICANT: Shen, Greg S.
; TITLE OF INVENTION: I-Superfamily Conotoxins
; FILE REFERENCE: 2314-238
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; CURRENT APPLICATION NUMBER: US/09/894,882
; CURRENT FILING DATE: 2001-06-29
; PRIOR APPLICATION NUMBER: US 60/
; PRIOR FILING DATE: 2000-06-30
; PRIOR APPLICATION NUMBER: US 60/243,410
; PRIOR FILING DATE: 2000-10-27
; PRIOR APPLICATION NUMBER: US 60/246,581
; PRIOR FILING DATE: 2000-11-08
; PRIOR APPLICATION NUMBER: US 60/247,714
; PRIOR FILING DATE: 2000-11-14
; PRIOR APPLICATION NUMBER: US 60/264,256
; PRIOR FILING DATE: 2001-01-29
; NUMBER OF SEQ ID NOS: 506
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 200
; LENGTH: 70
; TYPE: PRT
; ORGANISM: Conus lynceus
US-09-894-882-200

Query Match          39.6%; Score 55.5; DB 10; Length 70;
Best Local Similarity 40.7%; Pred. No. 0.35;
Matches 11; Conservative 0; Mismatches 15; Indels 1; Gaps 1;

OY 1 CRXNOKCFQHLDDCCSXKCNXXNXCVCV 27
DB 39 CFNAGVKCDNH-SDCEDPFCYDNTVCV 64

RESULT 13
US-09-894-882-305
; Sequence 305, Application US/09894882
; Patent No. US20020102607A1
; GENERAL INFORMATION:
; APPLICANT: University of Utah Research Foundation
; APPLICANT: Cognetix, Inc.
; APPLICANT: Walker, Craig S.
; APPLICANT: Shetty, Reshma
; APPLICANT: Jimenez, Elsie C.
; APPLICANT: McIntosh, J. Michael
; APPLICANT: Olivera, Baldomero M.
; APPLICANT: Watkins, Maren
; APPLICANT: Jones, Robert M.
; APPLICANT: Shen, Greg S.
; TITLE OF INVENTION: I-Superfamily Conotoxins
; FILE REFERENCE: 2314-238
; CURRENT APPLICATION NUMBER: US/09/894, 882
; CURRENT FILING DATE: 2001-06-29
; PRIOR APPLICATION NUMBER: US 60/
; PRIOR FILING DATE: 2000-06-30
; PRIOR APPLICATION NUMBER: US 60/243,410
; PRIOR FILING DATE: 2000-10-27
; PRIOR APPLICATION NUMBER: US 60/246,581
; PRIOR FILING DATE: 2000-11-08
; PRIOR APPLICATION NUMBER: US 60/247,714
; PRIOR FILING DATE: 2000-11-14
; PRIOR APPLICATION NUMBER: US 60/264,256
; PRIOR FILING DATE: 2001-01-29
; NUMBER OF SEQ ID NOS: 506
; SOFTWARE: PatentIn version 3.0
; SEQ ID NO 305
; LENGTH: 75
; TYPE: PRT
; ORGANISM: Conus aulicus
US-09-894-882-305

Query Match          39.6%; Score 55.5; DB 10; Length 75;
Best Local Similarity 33.3%; Pred. No. 0.37;
Matches 9; Conservative 4; Mismatches 13; Indels 1; Gaps 1;

OY 1 CRXNOKCFQHLDDCCSXKCNXXNXCVCV 27
DB 39 CSMSGQEC-KHVSDDCGSFCCVGRCL 64
```

RESULT 14  
US-09-894-882-369  
; Sequence 369, Application US/09894882  
; Patent No. US20020102607A1  
; GENERAL INFORMATION:  
; APPLICANT: University of Utah Research Foundation  
; APPLICANT: Cognetix, Inc.  
; APPLICANT: Walker, Craig S.  
; APPLICANT: Shetty, Reshma  
; APPLICANT: Jimenez, Elsie C.  
; APPLICANT: McIntosh, J. Michael  
; APPLICANT: Olivera, Baldomero M.  
; APPLICANT: Watkins, Maeren  
; APPLICANT: Jones, Robert M.  
; TITLE OF INVENTION: I-Superfamily Conotoxins  
; FILE REFERENCE: 2314-238  
; CURRENT APPLICATION NUMBER: US/09/894,882  
; PRIOR FILING DATE: 2001-06-29  
; PRIOR APPLICATION NUMBER: US 60/  
; PRIOR FILING DATE: 2000-06-30  
; PRIOR APPLICATION NUMBER: US 60/243,410  
; PRIOR FILING DATE: 2000-10-27  
; PRIOR APPLICATION NUMBER: US 60/246,581  
; PRIOR FILING DATE: 2000-11-08  
; PRIOR APPLICATION NUMBER: US 60/247,714  
; PRIOR FILING DATE: 2000-11-14  
; PRIOR APPLICATION NUMBER: US 60/264,256  
; PRIOR FILING DATE: 2001-01-29  
; NUMBER OF SEQ ID NOS: 506  
; SOFTWARE: PatentIn version 3.0  
; SEQ ID NO 369  
; LENGTH: 36  
; TYPE: PRT  
; ORGANISM: Conus betulinus  
US-09-894-882-369

Query Match 38.9%; Score 54.5; DB 10; Length 36;  
Best Local Similarity 37.0%; Pred. No. 0.26;  
Matches 10; Conservative 3; Mismatches 13; Indels 1; Gaps 1;

QY 1 CRXNKCFOHLDCCSXXCNXNXCVCV 27  
DB 2 CLSLGRCERH-SDCCGYLCCFYDKCV 27

RESULT 15  
US-09-894-882-167  
; Sequence 167, Application US/09894882  
; Patent No. US20020102607A1  
; GENERAL INFORMATION:  
; APPLICANT: University of Utah Research Foundation  
; APPLICANT: Cognetix, Inc.  
; APPLICANT: Walker, Craig S.  
; APPLICANT: Shetty, Reshma  
; APPLICANT: Jimenez, Elsie C.  
; APPLICANT: McIntosh, J. Michael  
; APPLICANT: Olivera, Baldomero M.  
; APPLICANT: Watkins, Maeren  
; APPLICANT: Jones, Robert M.  
; APPLICANT: Shen, Greg S.  
; TITLE OF INVENTION: I-Superfamily Conotoxins  
; FILE REFERENCE: 2314-238  
; CURRENT APPLICATION NUMBER: US/09/894,882  
; PRIOR FILING DATE: 2001-06-29  
; PRIOR APPLICATION NUMBER: US 60/  
; PRIOR FILING DATE: 2000-06-30  
; PRIOR APPLICATION NUMBER: US 60/243,410  
; PRIOR FILING DATE: 2000-10-27  
; PRIOR APPLICATION NUMBER: US 60/246,581  
; PRIOR FILING DATE: 2000-11-08  
; PRIOR APPLICATION NUMBER: US 60/247,714  
; PRIOR FILING DATE: 2000-11-14  
; PRIOR APPLICATION NUMBER: US 60/264,256  
; PRIOR FILING DATE: 2001-01-29  
; NUMBER OF SEQ ID NOS: 506  
; SOFTWARE: PatentIn version 3.0  
; SEQ ID NO 167  
; LENGTH: 73  
; TYPE: PRT  
; ORGANISM: Conus betulinus  
US-09-894-882-167

Query Match 38.9%; Score 54.5; DB 10; Length 73;  
Best Local Similarity 37.0%; Pred. No. 0.49;  
Matches 10; Conservative 3; Mismatches 13; Indels 1; Gaps 1;

; PRIOR APPLICATION NUMBER: US 60/247,714  
; PRIOR FILING DATE: 2000-11-14  
; PRIOR APPLICATION NUMBER: US 60/264,256  
; PRIOR FILING DATE: 2001-01-29  
; NUMBER OF SEQ ID NOS: 506  
; SOFTWARE: PatentIn version 3.0  
; SEQ ID NO 167  
; LENGTH: 73  
; TYPE: PRT  
; ORGANISM: Conus betulinus  
US-09-894-882-167

QY 1 CRXNKCFOHLDCCSXXCNXNXCVCV 27  
DB 39 CLSLGRCERH-SDCCGYLCCFYDKCV 64

Search completed: January 14, 2003, 18:30:04  
Job time : 11 secs

GenCore version 5.1.3  
Copyright (c) 1993 - 2003 CompuGen Ltd.

OM protein - protein search, using sw model

Run on: January 14, 2003, 18:27:06 ; Search time 15 Seconds  
(without alignments)  
173.042 Million cell updates/sec

Title: US-09-666-837B-1-COPY

Perfect score: 140

Sequence: 1 CRXNOKCFQHLDDCCSXCNXXNXC 27

Scoring table: BLOSUM62

Gapop 10.0 , Gapext 0.5

Searched: 283224 seqs, 96134422 residues

Total number of hits satisfying chosen parameters: 283224

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Database : PIR\_73:\*

1: PIR1:\*

2: PIR2:\*

3: PIR3:\*

4: PIR4:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	137	90.7	27	2	A58997 kappa-conotoxin PV
2	60	42.9	26	2	C44379 omega-conotoxin SV
3	56	40.0	2524	2	A35844 Notch protein - Af
4	55	39.3	2703	1	A24420 Notch protein - fr
5	52	37.1	1964	2	T09059 Notch4 - mouse
6	52	37.1	2437	2	S42612 transmembrane prot
7	52	37.1	2555	2	A40043 Notch protein homo
8	51	36.4	2531	2	S18188 Notch-1 protein -
9	51	36.4	2531	2	A46019 omega-conotoxin MV
10	50	35.7	29	2	JH0699 Notch B protein -
11	50	35.7	354	2	T22274 Notch B protein -
12	50	35.7	1203	2	A48175 Notch B protein -
13	50	35.7	2471	2	A48128 Notch B protein -
14	49	35.0	358	2	E86452 Notch B protein -
15	49	35.0	601	2	T22025 Notch B protein -
16	49	35.0	601	2	D89711 Notch B protein -
17	49	35.0	2318	2	S45306 Notch B protein -
18	49	35.0	2321	2	S78549 Notch B protein -
19	49	35.0	2352	2	T30201 Notch B protein -
20	49	35.0	3623	2	T08618 Notch B protein -
21	48.5	34.6	1208	2	T27822 Notch B protein -
22	48	34.3	293	2	B26637 Notch B protein -
23	48	34.3	1372	2	T25933 Notch B protein -
24	48	34.3	2139	2	A35672 Notch B protein -
25	48	34.3	2531	2	T30707 Notch B protein -
26	47.5	33.9	53	2	T30499 Notch B protein -
27	47.5	33.9	53	2	T10405 Notch B protein -
28	47	33.6	25	2	JH0700 Notch B protein -
29	47	33.6	29	2	B43620 Notch B protein -

30	47	33.6	832	2	A31246 neurogenic protein
31	47	33.6	833	2	S19087 gene Delta protein
32	47	33.6	880	2	S00670 neurogenic repeat
33	47	33.6	1064	2	A40136 fibropellin Ia - s
34	47	33.6	1466	2	B36655 silt protein 2 pre
35	47	33.6	1480	2	A36655 silt protein 1 pre
36	46.5	33.2	53	2	C72850 Notch B protein -
37	46	32.9	25	2	JH0701 Notch B protein -
38	46	32.9	644	2	S64135 Notch B protein -
39	46	32.9	722	2	T48324 Notch B protein -
40	46	32.9	1687	2	T30176 Notch B protein -
41	45.5	32.5	99	2	T26416 Notch B protein -
42	45.5	32.5	503	2	G85432 Notch B protein -
43	45	32.1	29	2	A58537 Notch B protein -
44	45	32.1	138	2	H64561 Notch B protein -
45	45	32.1	570	2	A48836 Notch B protein -

## ALIGNMENTS

## RESULT 1

A58997 kappa-conotoxin PVIIA - cone shell (Conus purpurascens)

N:Alternate names: fln-popping peptide

C:Species: Conus purpurascens (purple cone)

C>Date: 23-Jul-1999 #sequence\_revision 23-Jul-1999 #text\_change 23-Jul-1999

C:Accession: A58997

R:Terlau, H.; Shon, K.J.; Grille, M.; Stocker, M.; Stuehmer, W.; Olivera, B.M.

Nature 381, 148-151, 1996

A:Title: Strategy for rapid immobilization of prey by a fish-hunting marine snail.

A:Reference number: A58997

A:Accession: A58997

A:Status: preliminary

A:Residues: 1-27 <PER>

C:Comment: This conotoxin blocks conductance of the Shaker potassium channel.

C:Keywords: hydroxyproline; neurotoxin; venom

F:4/Modified site: 4-hydroxyproline (Pro) #status experimental

Query Match	90.7%	Score 127;	DB 2;	Length 27;
Best Local Similarity	77.8%	Pred. No. 6.6e-10;		
Matches	21;	Conservative	0;	Mismatches 6;
		Indels	0;	Gaps 0;

## RESULT 2

C44379 CRXNOKCFQHLDDCCSXCNXXNXC 27

DB 1 CRXNOKCFQHLDDCCSXCNXXNXC 27

C:Accession: C44379

C:Species: Conus striatus (striated cone)

C>Date: 31-Dec-1993 #sequence\_revision 31-Dec-1993 #text\_change 15-Sep-2000

R:Ramilo, C.A.; Zafaralla, G.C.; Nadeadi, L.; Hammerland, L.G.; Yoshikami, D.; Gray,

Biochemistry 31, 9919-9926, 1992

A:Title: Novel alpha- and omega-conotoxins from Conus striatus venom.

A:Reference number: A44379; MUID:93003172; PMID:1390774

A:Accession: C44379

A:Molecule type: protein

A:Residues: 1-26 <RAM>

A:Cross-references: CAS:143306-19-8

A:Experimental source: venom

A>Note: sequence extracted from NCBI backbone (NCBIP:116002); structure confirmed by

submitted to the Brookhaven Protein Data Bank, August 1996

A:Reference number: A67649; PDB:1WJ

A:Contents: annotation; conformation by (1)H-NMR, residues 1-26

J. Mol. Biol. 263, 297-310, 1996

A:Title: A consensus structure for omega-conotoxins with different selectivities for

A:Reference number: A58619; MUID:97070382; PMID:8913308  
 A:Contents: annotation; conformation by (1)H-NMR  
 A:Comment: This omega-conotoxin blocks presynaptic calcium channels.  
 C:Superfamily: omega-conotoxin  
 C:Keywords: acetylcholine release inhibition; amidated carboxyl end; calcium channel int  
 F:1-16-20,15-26/Disulfide bonds: #status predicted  
 F:26/Modified site: amidated carboxyl end (Cys) #status experimental

Query Match 42.9%; Score 60; DB 2; Length 26;  
 Best Local Similarity 34.6%; Pred. No. 0.21;  
 Matches 9; Conservative 3; Mismatches 14; Indels 0; Gaps 0;

OY 1 CRXNQCFOHLDCCSXKXNXXNCV 26  
 Db 1 CKLKGCSCRTSYDCCSCGCRSGKC 26

## RESULT 3

A35844  
 Xotch protein - African clawed frog  
 C:Species: Xenopus laevis (African clawed frog)  
 C>Date: 12-Oct-1990 #sequence\_revision 12-Oct-1990 #text\_change 02-Aug-2002  
 C:Accession: A35844  
 R:Coffman, C.; Harris, W.; Kintner, C.  
 Science 249, 1438-1441, 1990  
 A>Title: Xotch, the Xenopus homolog of Drosophila notch.  
 A:Reference number: A35844; MUID:90385285; PMID:2402639  
 A:Accession: A35844  
 A>Status: preliminary; nucleic acid sequence not shown; not compared with conceptual tra

A:Molecule type: mRNA  
 A:Residues: 1-2524 <COF>  
 C:Superfamily: notch protein; ankyrin repeat homology; EGF homology  
 C:Keywords: transmembrane protein  
 F:146-177/Domain: EGF homology <EGX1>  
 F:184-215/Domain: EGF homology <EGF1>  
 F:222-254/Domain: EGF homology <EGF2>  
 F:436-487/Domain: EGF homology <EGX2>  
 F:757-788/Domain: EGF homology <EGF3>  
 F:1025-1056/Domain: EGF homology <EGX3>  
 F:1924-1956/Domain: ankyrin repeat homology <AN1>  
 F:1957-1989/Domain: ankyrin repeat homology <AN2>  
 F:1991-2023/Domain: ankyrin repeat homology <AN3>  
 F:2024-2056/Domain: ankyrin repeat homology <AN4>  
 F:2057-2089/Domain: ankyrin repeat homology <AN5>

Query Match 40.0%; Score 56; DB 2; Length 2524;  
 Best Local Similarity 40.9%; Pred. No. 14;  
 Matches 9; Conservative 3; Mismatches 10; Indels 0; Gaps 0;

OY 6 QKCFQHLDDCCSXKXNXXNCV 27  
 Db 252 QNCEINIDDCPSNCRNGCTCV 273

## RESULT 4

A24420  
 notch protein - fruit fly (Drosophila melanogaster)  
 N:Alternate names: neurogenic repetitive locus protein  
 C:Species: Drosophila melanogaster  
 C>Date: 10-Sep-1999 #sequence\_revision 10-Sep-1999 #text\_change 10-Sep-1999  
 C:Accession: A24420; A24768; S09358; A05267  
 R:Kidd, S.; Kelley, M.R.; Young, M.W.  
 Mol. Cell. Biol. 6, 3094-3108, 1986

A:Reference number: A24420; MUID:87064624; PMID:3097517  
 A:Accession: A24420

A:Molecule type: DNA  
 A:Residues: 1-2703 <KID>  
 A:CROSS-references: GB:K03508; NID:g157991; PIDN:AAA28725.1; PID:g157993  
 R:Marathon, K.A.; Johansen, K.M.; Xu, T.; Artavanis-Tsakonas, S.

Cell 43, 567-581, 1985  
 A:Reference number: A24768; MUID:86079539; PMID:3935325  
 A:Accession: A24768  
 A:Molecule type: mRNA

A:Residues: 1-48, 'I', 50-118, 'R', 120-230, 'I', 232-256, 'N', 258-266, 'A', 268-872, 'R', 874-9  
 A>Note: the authors translated the codon ATC for residue 49 as Thr, ATT for residue 2  
 R:Nautz, D.  
 Nucleic Acids Res. 17, 6463-6471, 1989

A>Title: Hypervariability of simple sequences as a general source for polymorphic DNA  
 A:Reference number: S09358; MUID:89385974; PMID:2780284  
 A:Accession: S09358  
 A:Molecule type: DNA  
 A:Residues: 2505-2551, 'Q'Q'Q', 2552-2576, 'E', 2578-2604 <TAN>  
 R:Marathon, K.A.; Yedvobnick, B.; Finnerty, V.G.; Artavanis-Tsakonas, S.

Cell 40, 55-62, 1985  
 A>Title: opa: a novel family of transcribed repeats shared by the Notch locus and oth  
 A:Reference number: A05267; MUID:85099329; PMID:2981631  
 A:Accession: A05267  
 A:Molecule type: DNA  
 A:Residues: 2504-2576, 'E', 2578-2611 <MHA2>

C:Genetics:  
 A:Gene: notch; opa  
 A:CROSS-references: FlyBase:FBgn0004647  
 A:Map position: 8.96-9.36

A:Introns: 53/3; 84/3; 171/3; 240/3; 283/3; 233/3; 2436/3; 2588/3  
 C:Superfamily: notch protein; ankyrin repeat homology; EGF homology  
 C:Keywords: differentiation; tandem repeat; transmembrane protein  
 F:27-43/Domain: transmembrane #status predicted <TMN1>  
 F:297-328/Domain: EGF homology <EGX1>  
 F:530-561/Domain: EGF homology <EGF1>  
 F:568-599/Domain: EGF homology <EGF2>  
 F:988-1019/Domain: EGF homology <EGX2>

F:1064-1095/Domain: EGF homology <EGF3>  
 F:1187-1218/Domain: EGF homology <EGX3>  
 F:1746-1762/Domain: transmembrane #status predicted <TMN2>  
 F:1950-1982/Domain: ankyrin repeat homology <AN1>  
 F:1983-2015/Domain: ankyrin repeat homology <AN2>  
 F:1988-2004/Domain: transmembrane #status predicted <TMN3>  
 F:2017-2049/Domain: ankyrin repeat homology <AN3>  
 F:2050-2082/Domain: ankyrin repeat homology <AN4>  
 F:2083-2115/Domain: ankyrin repeat homology <AN5>  
 F:2538-2568/Region: glutamine-rich

F:2538-2568/Domain: neurogenic repetitive element #status predicted <OPA>  
 Query Match 39.3%; Score 55; DB 1; Length 2703;  
 Best Local Similarity 36.4%; Pred. No. 19;  
 Matches 8; Conservative 4; Mismatches 10; Indels 0; Gaps 0;

OY 6 QKCFQHLDDCCSXKXNXXNCV 27  
 Db 824 QKCFINIDDCVTPNCRNGCTCI 845

## RESULT 5

T09059  
 notch4 - mouse  
 C:Species: Mus musculus (house mouse)  
 C>Date: 11-Jun-1999 #sequence\_revision 11-Jun-1999 #text\_change 11-Jan-2000  
 C:Accession: T09059  
 R:Rowen, L.; Mahairas, G.; Qin, S.; Ahearn, M.E.; Dankers, C.; Lasky, S.; Loretz, C.;  
 submitted to the EMBL Data Library, October 1997

A:Description: Sequence of the mouse major histocompatibility locus class III region.  
 A:Reference number: Z16543  
 A:Accession: T09059  
 A>Status: preliminary; translated from GB/EMBL/DBJ

A:Molecule type: DNA  
 A:Residues: 1-1964 <ROW>  
 A:CROSS-references: EMBL:AF030001; NID:g2564945; PID:g2564947

C:Genetics:  
 A:Gene: notch4

A:Map position: 17  
 A:Introns: 22/1; 49/2; 148/1; 264/1; 305/1; 384/1; 436/1; 501/1; 539/1; 577/1; 618/1;  
 1679/3; 1729/1; 1761/3  
 C:Superfamily: unassigned EGF-related proteins; EGF homology  
 C:Keywords: receptor; signal transduction  
 F:514-545/Domain: EGF homology <EGF>

Query Match 37.1%; Score 52; DB 2; Length 1964;  
Best Local Similarity 35.0%; Pred. No. 37;  
Matches 7; Conservative 5; Mismatches 8; Indels 0; Gaps 0;

OY 8 CF0HLDDCCSXXCNXXNXC 27  
| : : : | | | : | : | : |  
DB 349 CEENIDDCAAATCAFGSTCI 368

## RESULT 6

S42612 transmembrane protein precursor - zebra fish

C:Species: Brachydanio rerio (zebra fish)

C:Date: 20-Feb-1995 #sequence\_revision 20-Feb-1995 #text\_change 02-Aug-2002

C:Accession: S42612

A:Title: A zebrafish homolog of the Drosophila neurogenic gene Notch and its pattern

A:Reference number: S42612; MUID:94128602; PMID:8297791

A:Accession: S42612

A:Molecule type: mRNA

A:Status: preliminary

A:Residues: 1-2437 <BIE>

C:Superfamily: notch protein; ankyrin repeat homology; EGF homology

F:1023-1054/Domain: EGF homology <EGF1>

F:1185-1216/Domain: EGF homology <EGF2>

F:1915-1947/Domain: ankyrin repeat homology <AN1>

F:1948-1980/Domain: ankyrin repeat homology <AN2>

F:1982-2014/Domain: ankyrin repeat homology <AN3>

F:2015-2047/Domain: ankyrin repeat homology <AN4>

F:2048-2080/Domain: ankyrin repeat homology <AN5>

Query Match 37.1%; Score 52; DB 2; Length 2437;  
Best Local Similarity 36.8%; Pred. No. 43;

Matches 7; Conservative 4; Mismatches 8; Indels 0; Gaps 0;

OY 8 CF0HLDDCCSXXCNXXNXC 26  
| : : : | | | : | : | : |  
DB 331 CSENIDDCASACSHGATC 349

## RESULT 7

A40043 notch protein homolog TAN-1 precursor - human

C:Species: Homo sapiens (man)

C:Date: 21-Apr-1992 #sequence\_revision 21-Apr-1992 #text\_change 02-Aug-2002

C:Accession: A40043

R:Ellisen, L.W.; Bird, J.; West, D.C.; Soreng, A.L.; Reynolds, T.C.; Smith, S.D.; Sklar, Cell 66, 649-661, 1991

A:Title: TAN-1, the human homolog of the Drosophila Notch gene, is broken by chromosomal

A:Reference number: A40043; MUID:1347367; PMID:1831692

A:Accession: A40043

A:Status: preliminary; nucleic acid sequence not shown; not compared with conceptual tra

A:Molecule type: mRNA

A:Residues: 1-2555 <DEL>

A:Cross-References: GB:M3980

C:Superfamily: notch protein; ankyrin repeat homology; EGF homology

F:261-292/Domain: EGF homology <EGF1>

F:494-525/Domain: EGF homology <EGF1>

F:987-1018/Domain: EGF homology <EGF2>

F:1146-1180/Domain: EGF homology <EGF3>

F:1187-1218/Domain: EGF homology <EGF3>

F:1233-1264/Domain: EGF homology <EGF3>

Query Match 37.1%; Score 52; DB 2; Length 2555;  
Best Local Similarity 36.4%; Pred. No. 45;

Matches 8; Conservative 3; Mismatches 11; Indels 0; Gaps 0;

OY 6 QKCF0HLDDCCSXXCNXXNXC 27  
| : : : | | | : | : | : |  
DB 252 QNCEENIDDCPGNNCKNGACV 273

## RESULT 8

S18188 notch protein homolog - rat

C:Species: Rattus norvegicus (Norway rat)

C:Date: 19-Feb-1994 #sequence\_revision 10-Nov-1995 #text\_change 02-Aug-2002

C:Accession: S18188

R:Weinmaster, G.; Roberts, V.J.; Lemke, G. Development 113, 199-205, 1991

A:Title: A homolog of Drosophila Notch expressed during mammalian development.

A:Reference number: S18188; MUID:92111383; PMID:1764995

A:Accession: S18188

A:Molecule type: mRNA

A:Residues: 1-2531 <WEI>

C:Superfamily: notch protein; ankyrin repeat homology; EGF homology

F:987-1018/Domain: EGF homology <EGF1>

F:1025-1056/Domain: EGF homology <EGF2>

F:1233-1264/Domain: EGF homology <EGF2>

F:1917-1949/Domain: ankyrin repeat homology <AN1>

F:1950-1982/Domain: ankyrin repeat homology <AN2>

F:1984-2016/Domain: ankyrin repeat homology <AN3>

F:2017-2049/Domain: ankyrin repeat homology <AN4>

F:2050-2082/Domain: ankyrin repeat homology <AN5>

Query Match 36.4%; Score 51; DB 2; Length 2531;  
Best Local Similarity 36.4%; Pred. No. 59;

Matches 8; Conservative 3; Mismatches 11; Indels 0; Gaps 0;

OY 6 QKCF0HLDDCCSXXCNXXNXC 27  
| : : : | | | : | : | : |  
DB 252 QNCEENIDDCPGNNCKNGACV 273

## RESULT 9

A46019 Notch-1 protein - mouse

C:Species: Mus musculus (house mouse)

C:Date: 22-Sep-1993 #sequence\_revision 18-Nov-1994 #text\_change 20-Sep-1999

C:Accession: A46019; S25144

R:del Amo, F.F.; Gendron-Maguire, M.; Swatek, P.J.; Jenkins, N.A.; Copeland, N.G.; G. Genomics 15, 259-264, 1993

A:Title: Cloning, analysis, and chromosomal localization of Notch-1, a mouse homolog

A:Reference number: A46019; MUID:93194170; PMID:8449489

A:Accession: A46019

A:Status: not compared with conceptual translation

A:Molecule type: nucleic acid

A:Residues: 1-2531 <DEL>

A:Cross-References: GB:Z11886; GB:S47228; NID:9288502; PIDN:CAA77941.1; PMID:9288503

A:Note: sequence extracted from NCBI backbone (NCBI:P127318)

R:Francisco del Amo, F.; Smith, D.E.; Swatek, P.J.; Gendron-Maguire, M.; Greenspan, R.J. submitted to the EMBL Data Library, April 1992

A:Description: Expression pattern of Notch, a mouse homolog of Drosophila Notch, sugg

A:Reference number: S25144

A:Accession: S25144

A:Molecule type: mRNA

A:Residues: 1551-2108, 'Q', 2110-2114, 'ALP', 2118-2170 <FRA>

A:Cross-References: EMBL:Z11886

C:Genetics: A:Gene: notch-1

Query Match 36.4%; Score 51; DB 2; Length 2531;  
Best Local Similarity 36.4%; Pred. No. 59;

Matches 8; Conservative 3; Mismatches 11; Indels 0; Gaps 0;

F:261-292/Domains: EGF homology <EG02>  
F:339-370/Domains: EGF homology <EG03>  
F:416-449/Domains: EGF homology <EGF3>  
F:456-487/Domains: EGF homology <EG04>  
F:494-525/Domains: EGF homology <EG05>  
F:532-563/Domains: EGF homology <EG06>  
F:607-638/Domains: EGF homology <EG07>  
F:682-713/Domains: EGF homology <EG08>  
F:757-788/Domains: EGF homology <EG09>  
F:795-826/Domains: EGF homology <EG10>  
F:873-904/Domains: EGF homology <EG11>  
F:911-942/Domains: EGF homology <EG12>  
F:949-980/Domains: EGF homology <EG13>  
F:987-1018/Domains: EGF homology <EG14>  
F:1025-1056/Domains: EGF homology <EG15>  
F:1063-1094/Domains: EGF homology <EG16>  
F:1149-1180/Domains: EGF homology <EG17>  
F:1187-1218/Domains: EGF homology <EG18>  
F:1233-1264/Domains: EGF homology <EG19>  
F:1352-1383/Domains: EGF homology <EG20>  
F:1391-1425/Domains: EGF homology <EG21>  
F:1917-1948/Domains: ankyrin repeat homology <AN1>  
F:1949-1981/Domains: ankyrin repeat homology <AN2>  
F:1983-2015/Domains: ankyrin repeat homology <AN3>  
F:2016-2048/Domains: ankyrin repeat homology <AN4>  
F:2049-2081/Domains: ankyrin repeat homology <AN5>

Query Match 36.4%; Score 51; DB 2; Length 2531;  
Best Local Similarity 36.4%; Pred. No. 59;

Matches 8; Conservative 3; Mismatches 11; Indels 0; Gaps 0;

Qy 6 OKCFQHLDDCCSXKCNXXKCV 27  
Db 252 QNCEENVDDCPGNCKNGACV 273

## RESULT 10

Omega-conotoxin MVIC precursor [validated] - cone shell (Conus magus) (fragment)

C/Species: Conus magus (magus cone)

C/Date: 17-Apr-1993 #sequence\_revision 11-Apr-1997 #text\_change 15-Sep-2000

C/Accession: JH0699; PC2380

R/Hillyard, D.R.; Monje, V.O.; Miltz, I.M.; Bean, B.P.; Nadasdi, L.; Ramachandran, J.; M

Neuron 9, 69-77, 1992

A/Title: A new cone peptide ligand for mammalian presynaptic Ca2+ channels.

A/Reference number: JH0699; MUID:92337922; PMID:1352986

A/Accession: JH0699

A/Molecule type: mRNA

A/Residues: 1-29 <HL>

A/Cross-references: GB:S40826; NID:9252126; PIDN:AA822674.1; PID:9252127

R/Nemoto, N.; Kubo, S.; Yoshida, T.; Chino, N.; Kimura, T.; Sakakibara, S.; Kyogoku, Y.;

Biochem. Biophys. Res. Commun. 207, 695-700, 1995

A/Title: Solution structure of omega-conotoxin MVIC determined by NMR.

A/Reference number: PC2380; MUID:95169113; PMID:7864862

A/Accession: PC2380

A/Molecule type: protein

A/Residues: 3-28 <MEM>

R/Farr-Jones, S.; Basus, V.J.

Submitted to the Brookhaven Protein Data Bank, December 1994

A/Reference number: A66297; PDB:1OMN

A/Contents: annotation: conformation by (1)H-NMR, residues 3-28

R/Farr-Jones, S.; Mijlanich, G.P.; Nadasdi, L.; Ramachandran, J.; Basus, V.J.

J. Mol. Biol. 248, 106-124, 1995

A/Title: Solution structure of omega-conotoxin MVIC, a high affinity of P-type calcium

A/Reference number: A58582; MUID:95248539; PMID:7732037

A/Contents: annotation: conformation by (1)H-NMR

C/Superfamily: omega-conotoxin

C/Keywords: acetylcholine release inhibition; amidated carboxyl end; calcium channel inh

F:3-28/Product: omega-conotoxin MVIC #status experimental <MAT>

F:3-18,10-22,17-28/Disulfide bonds: #status experimental

F:28/Modified site: amidated carboxyl end (Cys) (amide in mature form from following gly

Query Match 35.7%; Score 50; DB 2; Length 29;

Best Local Similarity 30.8%; Pred. No. 4.2;  
Matches 8; Conservative 3; Mismatches 15; Indels 0; Gaps 0;

Qy 1 CRINOKFOHLDCCSXKCNXXKNC 26  
Db 3 CKKGAPCRKTMDDCCSGSGRGK 28

## RESULT 11

hypochemical protein F46B3.9 - Caenorhabditis elegans

C/Species: Caenorhabditis elegans

C/Date: 15-Oct-1999 #sequence\_revision 15-Oct-1999 #text\_change 15-Oct-1999

C/Accession: T22274

R/Almscough, R.

submitted to the EMBL Data Library, November 1996

A/Reference number: Z19541

A/Accession: T22274

A/Status: preliminary; translated from GB/EMBL/DBJ

A/Molecule type: DNA

A/Residues: 1-354 <WTL>

A/Cross-references: EMBL:281540; PIDN:CA804398.1; GSPDB:GN00023; CESP:F46B3.9

A/Experimental source: clone F46B3

C/Genetics:

A/Gene: CESP:F46B3.9

A/Map position: 5

A/Insertions: 23/1; 55/1; 82/1; 112/1; 142/1; 170/1; 193/1; 223/1; 299/1

Query Match 35.7%; Score 50; DB 2; Length 354;

Best Local Similarity 32.1%; Pred. No. 22;

Matches 9; Conservative 4; Mismatches 13; Indels 2; Gaps 1;

Qy 1 CRINX--OKCFQHLDDCCSXKCNXXKNC 26  
Db 158 CKLVGSPKCPVPELDQCSHKCSIGSHC 185

## RESULT 12

Notch B protein - mouse (fragment)

N/Alternate names: Notch homolog

C/Species: Mus musculus (house mouse)

C/Date: 21-Jan-1994 #sequence\_revision 05-Jan-1996 #text\_change 20-Sep-1999

C/Accession: A49175; P11570; S32113

R/Lardelli, M.; Lendahl, U.

Exp. Cell Res. 204, 364-372, 1993

A/Title: Notch A and Notch B -two mouse Notch homologues coexpressed in a wide variety

A/Reference number: A49175; MUID:93178563; PMID:8440332

A/Accession: A49175

A/Status: preliminary; nucleic acid sequence not shown

A/Molecule type: mRNA

A/Residues: 1-1203 <LAR>

A/Cross-references: EMBL:X68279; NID:9287989; PIDN:CAA48340.1; PID:9287990

A/Experimental source: embryo

A/Note: sequence extracted from NCBI backbone (NCBI:P126158)

C/Comment: This protein has many EGF repeats and 11n-12/Notch repeats.

C/Superfamily: unassigned ankyrin repeat proteins; ankyrin repeat homology; EGF homol

F:143-174/Domains: EGF homology <EGX1>

F:148-174/Domains: EGF homology <EGX1>

F:148-513/Domains: EGF homology <EGF1>

F:560-591/Domains: EGF homology <EGX2>

F:674-705/Domains: EGF homology <EGX2>

F:712-743/Domains: EGF homology <EGF3>

F:836-867/Domains: EGF homology <EGX3>

Query Match 35.7%; Score 50; DB 2; Length 1203;

Best Local Similarity 30.0%; Pred. No. 49;

Matches 6; Conservative 5; Mismatches 9; Indels 0; Gaps 0;

Qy 8 CFQHLDDCCSXKCNXXKCV 27  
Db 18 CSENIDCAVASCYPCSTCI 37







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OM protein - protein search, using sw model

Run on: January 14, 2003, 18:17:10 ; Search time 11 Seconds

(without alignments)  
101.806 Million cell updates/sec

Title: US-09-666-837B-1-COPY

Perfect score: 140  
Sequence: 1 CRXNQCfQhLDCCSXXCNXNXC 27

Scoring table: BLOSUM62  
Gapop 10.0 , Gapext 0.5

Searched: 112892 seqs, 41476328 residues

Total number of hits satisfying chosen parameters: 112892

Minimum DB seq length: 0

Maximum DB seq length: 200000000

Post-Processing: Minimum Match 0%

Maximum Match 100%

Listing first 45 summaries

Database : SwissProt\_40:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	127	90.7	72	1	CKX7_CONPU
2	60	42.9	72	1	CKOB_CONST
3	56	40.0	2524	1	NORC_XENLA
4	55	39.3	26	1	CKOC_CONCT
5	55	39.3	2703	1	NORC_DROME
6	53	37.9	73	1	CKOD_CONCT
7	52	37.1	1964	1	NTC4_MOUSE
8	52	37.1	2437	1	NTC1_BRARE
9	52	37.1	2556	1	NTC1_HUMAN
10	51	36.4	589	1	DL3_RAT
11	51	36.4	592	1	DL3_MOUSE
12	51	36.4	618	1	DL3_HUMAN
13	51	36.4	2003	1	NTC4_HUMAN
14	51	36.4	2531	1	NTC1_MOUSE
15	51	36.4	2531	1	NTC1_RAT
16	50	35.7	29	1	CKOC_CONMA
17	50	35.7	2470	1	NTC2_MOUSE
18	50	35.7	2471	1	NTC2_HUMAN
19	50	35.7	2471	1	NTC2_RAT
20	49	35.0	1202	1	JAG2_RAT
21	49	35.0	1238	1	JAG2_HUMAN
22	49	35.0	1247	1	JAG2_MOUSE
23	49	35.0	2318	1	NTC3_MOUSE
24	49	35.0	2319	1	NTC3_RAT
25	49	35.0	2321	1	NTC3_HUMAN
26	48	34.3	2139	1	CRB_DROME
27	47.5	33.9	53	1	CTIL_NPYOP
28	47	33.6	71	1	CKOA_CONMA
29	47	33.6	723	1	DL1_HUMAN
30	47	33.6	833	1	DL1_MOUSE
31	47	33.6	1064	1	FBPL_STRPU
32	47	33.6	1480	1	SLIT_DROME
33	46.5	33.2	53	1	CTL_NPVAC

34	46	32.9	25	1	CKOB_CONMA	P05485	conus magus
35	46	32.9	644	1	YGM4_YEAST	P53129	saccharomyc
36	46	32.9	714	1	DL1_RAT	P97677	rattus norv
37	46	32.9	722	1	DL1_MOUSE	061483	mus musculu
38	45	32.1	29	1	CKOD_CONMA	026350	conus magus
39	45	32.1	399	1	LHX5_BRARE	P52889	brachydantio
40	45	32.1	570	1	FBP3_STRPU	P49013	strongyloce
41	45	32.1	1213	1	JAG3_BRARE	090524	brachydantio
42	45	32.1	1218	1	JAG1_HUMAN	P78504	homo sapien
43	45	32.1	1218	1	JAG1_MOUSE	09qxx0	mus musculu
44	44	31.4	268	1	ITLB_RABIT	P14628	oryctolagus
45	44	31.4	402	1	LHX5_XENLA	P37137	xenopus lae

## ALIGNMENTS

RESULT 1  
CKX7\_CONPU STANDARD; PRT; 72 AA.  
AC P56633;  
DT 15-DEC-1998 (Rel. 37, Created)  
DT 15-JUN-2002 (Rel. 41, Last sequence update)  
DT 15-JUN-2002 (Rel. 41, Last annotation update)  
DE Kappa-conotoxin PVIIA precursor (Pin-popping peptide).  
OS Conus purpurascens (Purple cone).  
OC Eukaryota; Metazoa; Mollusca; Gastropoda; Caenogastropoda;  
NCBI\_TaxID=41690;  
RN [1]  
RP SEQUENCE FROM N.A., AND SYNTHESIS.  
RX MEDLINE=98079023; PubMed=9417043;  
RA Shon K.-J., Stocker M., Terlau H., Stuehmer W., Jacobsen R.B.,  
Walker C.S., Grille M.M., Watkins M., Hillyard D.R., Gray W.R.,  
Olivera B.M.;  
RT "Kappa-conotoxin PVIIA is a peptide inhibiting the shaker K+  
channel.";  
RL J. Biol. Chem. 273:33-38(1998).  
RN [2]  
RP SEQUENCE OF 46-72, AND SYNTHESIS.  
RX PubMed=12074021;  
RA Terlau H., Shon K.-J., Grille M.M., Stocker M., Stuehmer W.,  
Olivera B.M.;  
RT "Strategy for rapid immobilization of prey by a fish-hunting marine  
snail.";  
RL Nature 381:148-151(1996).  
RN [3]  
RP STRUCTURE BY NMR.  
RX TISSUE=Venom;  
MEDLINE=98104087; PubMed=9438859;  
RA Scanlon M.J., Naranjo D., Thomas L., Alewood P.F., Lewis R.J.,  
Craik D.J.;  
RT "Solution structure and proposed binding mechanism of a novel  
potassium channel toxin kappa-conotoxin PVIIA.";  
RL Structure 5:1585-1597(1997).  
RN [4]  
RP STRUCTURE BY NMR.  
RX MEDLINE=9821795; PubMed=9548922;  
RA Savarin P., Guenenez M., Gilquin B., Lamthanh H., Gasparini S.,  
Zinn-Justin S., Menez A.;  
RT "Three-dimensional structure of kappa-conotoxin PVIIA, a novel  
potassium channel-blocking toxin from cone snails.";  
RL Biochemistry 37:5407-5416(1998).  
RN [5]  
RP MUTAGENESIS OF ARG-47; ILE-48; PRO-49; ASN-50; GLN-51; PHE-54;  
PHE-54; GLN-55; HIS-56; LEU-57; ASP-58; ASP-59; SER-62; ARG-63;  
LYS-64; ARG-67; PHE-68; ASN-69 AND LYS-70.  
RX PubMed=10818087;  
RA Jacobsen R.B., Koch E.D., Lange-Malecki B., Stocker M., Verhey J.,  
Van Wagoner R.M., Vozovkina A., Olivera B.M., Terlau H.;  
RT "Single amino acid substitutions in kappa-conotoxin PVIIA disrupt  
interaction with the shaker K+ channel.";  
RL J. Biol. Chem. 275:24639-24644(2000).

[6]  
 BLOCKADE OF SHAKER CHANNEL BY PVIIA.  
 PubMed-10398696;  
 Terlau H., Boccaccio A., Olivera B.M., Conli F.;  
 "Type block of Shaker K<sup>+</sup> channels by kappa-conotoxin PVIIA is state dependent."; *Gen. Physiol.* 114:125-140(1999).  
 J. Gen. Physiol. 114:125-140(1999).  
 (7)  
 MODEL OF THE SHAKER-PVIIA INTERACTION.  
 PubMed-11820396;  
 Moran O.;  
 "Molecular stimulation of the interaction of kappa-conotoxin-PVIIA with the Shaker potassium channel pore."; *Eur. Biophys. J.* 30:528-536(2001).  
 (8)  
 BLOCKADE OF SHAKER CHANNEL BY PVIIA.  
 PubMed-12023223;  
 Naranjo D.;  
 "Inhibition of single Shaker K channels by kappa-conotoxin-PVIIA."; *Biophys. J.* 82:3003-3011(2002).  
 -1- FUNCTION: Kappa-conotoxins bind and inhibit voltage-sensitive potassium channels. The rat brain voltage-gated potassium channel protein Kv1.1 is resistant to this toxin, but the voltage-gated potassium channel protein Shaker (Drosophila) is sensitive. The interaction site between the Shaker channel and this toxin is within the S5-S6 loop of the Shaker channel. In fish, this toxin induces hyperactivity, followed by continuous contraction and extension of major fins, without immobilization or death. Injection of this peptide together with the delta-conotoxin PVIA causes the sudden tetanus of prey (STOP) syndrome, which is a single, lethal "fin-pop" in envenomated fish. In mice, induces hyperactivity.  
 -1- SUBCELLULAR LOCATION: Secreted.  
 -1- TISSUE SPECIFICITY: Expressed by the venom duct.  
 -1- MASS SPECTROMETRY: MW=3268.4; METHOD=FAV.  
 -1- SIMILARITY: BELONGS TO THE O-SUPERFAMILY OF CONOTOXINS.  
 -1- CAUTION: Because analogs resulting of mutagenesis of HRP-49, Asn-50, Leu-57 and Asp-59 gave very low yields upon folding, the results of mutagenesis on these residues should be interpreted with caution.  
 PDB: 1AV3; 18-NOV-98.  
 PDB: 1KCP; 14-OCT-98.  
 DR Neurotoxin: Toxin: Potassium channel inhibitor; Hydroxylation: 3D-structure: Signal.  
 KW SIGNAL 1 22  
 FT PROPER 23 45  
 FT PEPTIDE 46 72  
 FT DISULFID 46 61  
 FT DISULFID 53 65  
 FT DISULFID 60 71  
 FT MOD\_RES 49 49  
 FT MODAGEN 47 47  
 FT MODAGEN 47 47  
 FT MODAGEN 48 48  
 FT MODAGEN 49 49  
 FT MODAGEN 50 50  
 FT MODAGEN 51 51  
 FT MODAGEN 52 52  
 FT MODAGEN 54 54  
 FT MODAGEN 55 55  
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 FT MODAGEN 56 56  
 FT MODAGEN 57 57  
 FT MODAGEN 58 58  
 FT MODAGEN 59 59  
 FT MODAGEN 62 62  
 FT MODAGEN 63 63  
 FT MODAGEN 64 64  
 FT MODAGEN 67 67  
 FT MODAGEN 68 68  
 FT MODAGEN 69 69  
 FT MODAGEN 70 70  
 FT MODAGEN 70 70  
 FT SEQUENCE 72 AA; 8317 MM; 53BFAF79EE751C16 CMC64;

Query Match 90.7%; Score 127; DB 1; Length 72;  
 Best Local Similarity 77.8%; Pred. No. 3e-11;  
 Matches 21; Conservative 0; Mismatches 6; Indels 0; Gaps 0;  
 QY 1 CRXNOKCFQHLDDCCSXKCNXNCV 27  
 ||| ||||| ||||| ||| |||  
 DB 46 CRIPNOKCFQHLDDCCSRKCNRFNKCVCV 72  
 RESULT 2  
 ID CXOB\_CONST STANDARD; PRT; 72 AA.  
 AC P28881; Q9UB25;  
 DT 01-DEC-1992 (Rel. 24, Created)  
 DT 16-OCT-2001 (Rel. 40, Last sequence update)  
 DT 15-JUN-2002 (Rel. 41, Last annotation update)  
 DE Omega-conotoxin SVIB precursor (SNX-183).  
 OS Conus striatus (Striated cone).  
 OC Eukaryota; Metazoa; Mollusca; Gastropoda; Caenogastropoda; Neogastropoda; Conoidea; Conidae; Conus.  
 OX NCBI\_TaxID=6493;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC TISSUE-Venom duct;  
 RX MEDLINE-20037955; PubMed-10573284;  
 RA Lu B.-S., Yu F., Zhao D., Huang P.-T., Huang C.-F.;  
 RT "Conopeptides from Conus striatus and Conus textile by cDNA cloning."; *Biophys. J.* 76:1139-1144(1999).  
 RL Peptides 20:1139-1144(1999).  
 RN [2]  
 RP SEQUENCE OF 46-71, AND SYNTHESIS.  
 RC TISSUE-Venom;  
 RX MEDLINE-93003172; PubMed-1390774;  
 RA Ramilo C., Zafaralla G.C., Nadesdi L., Hammerland L.G., Yoshikami D., Gray W.R., Kristipati R., Ramachandran J., Miljanich G., Olivera B.M., Cruz L.J.;  
 RT "Novel alpha- and omega-conotoxins from Conus striatus venom."; *Biochemistry* 31:9919-9926(1992).  
 RL [3]  
 RP STRUCTURE BY NMR.  
 RX MEDLINE-97070382; PubMed-89133308;  
 RA Nielsen K.J., Thomas L., Lewis R.J., Alewood P.F., Craik D.J.;  
 RT "A consensus structure for omega-conotoxins with different selectivities for voltage-sensitive calcium channel subtypes: comparison of MVIIA, SVIB and SNX-202."; *J. Mol. Biol.* 263:297-310(1996).  
 RL J. Mol. Biol. 263:297-310(1996).  
 CC -1- FUNCTION: Omega-conotoxins act at presynaptic membranes, they bind and block voltage-sensitive calcium channels (VSCC). This toxin blocks N-, P-, and Q-type calcium channels.  
 CC -1- SUBCELLULAR LOCATION: Secreted.  
 CC -1- TISSUE SPECIFICITY: Expressed by the venom duct.  
 CC -1- SIMILARITY: BELONGS TO THE O-SUPERFAMILY OF CONOTOXINS. OMEGA-TYPE FAMILY.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and the EMBL outstation at the European Bioinformatics Institute. There are no restrictions on its use by non-profit institutions as long as its content is in no way modified and this statement is not removed. Usage by and for commercial entities requires a license agreement (see <http://www.isb-sib.ch/announce/> or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
 CC -----  
 CC EMBL: AF146346; AAD31906.1; -  
 DR PIR: CA4379; CA4379.  
 DR PDB: 1MWJ; 12-AUG-97.  
 DR InterPro: IPR004214; Conotoxin.  
 DR Pfam: PF02950; Conotoxin; 1.  
 KW Presynaptic neurotoxin; Neurotoxin; Toxin; Calcium channel inhibitor; Amidation; Signal; 3D-structure.  
 FT SIGNAL 1 22  
 FT PROPER 23 45  
 FT PEPTIDE 46 71  
 FT DISULFID 46 61  
 FT DISULFID 46 61  
 FT OMEGA-CONOTOXIN SVIB.

FT DISULFID 53 65  
 FT DISULFID 60 71  
 FT MOD.RES 71 71  
 SO SEQUENCE 72 AA; 7741 MW; 1F753546AAD39908 CRC64;  
 Query Match 42.9%; Score 60; DB 1; Length 72;  
 Best Local Similarity 34.6%; Pred. No. 0.044;  
 Matches 9; Conservative 3; Mismatches 14; Indels 0; Gaps 0;  
 Oy 1 CRXNOKFOHLDCCSXCNXXNC 26  
 Db 46 CKLKGSCRTSTDCSGSGSGK 71  
 RESULT 3  
 NOTC\_XENLA STANDARD; PRT: 2524 AA.  
 AC P21783;  
 DT 01-MAY-1991 (Rel. 18, Created)  
 DT 01-OCT-1996 (Rel. 34, Last sequence update)  
 DT 15-JUN-2002 (Rel. 41, Last annotation update)  
 DE Neurogenic locus notch protein precursor (NOTCH protein).  
 GN NOTCH.  
 OS Xenopus laevis (African clawed frog).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipidoidea; Pipidae;  
 OC Xenopodidae; Xenopus.  
 OX NCBI\_TaxID=8355;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=90385285; PubMed=2402639;  
 RA Coffman C., Harris W., Kintner C.;  
 RT "Notch, the xenopus homolog of Drosophila notch."; Science 249:1438-1441(1990).  
 RL Science 249:1438-1441(1990).  
 RN [2]  
 RP REVISIONS TO 1759-1782.  
 RA Kintner C.;  
 RL Submitted (JUN-1996) to the EMBL/GenBank/DBJ databases.  
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -1- DEVELOPMENTAL STAGE: EXPRESSED ALMOST UNIFORMLY IN EARLY EMBRYOS.  
 CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 CC -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
 CC -1- SIMILARITY: CONTAINS 6 ANK REPEATS.  
 CC -----  
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 DR EMBL: M33874; AAB02039.1; -  
 DR PIR: A35844; A35844.  
 DR HSP: P00740; IEDM.  
 DR InterPro: IPR002110; ANK.  
 DR InterPro: IPR000152; Asx\_hydroxyl.  
 DR InterPro: IPR000561; EGF-like.  
 DR InterPro: IPR000742; EGF\_2.  
 DR InterPro: IPR001881; EGF\_Ca.  
 DR InterPro: IPR001438; EGF\_LI.  
 DR InterPro: IPR000800; Notch.  
 DR Pfam: PF00008; EGF; 36.  
 DR Pfam: PF00023; ank; 6.  
 DR Pfam: PF00066; notch; 3.  
 DR PRINTS: PR00010; EGFBL00.  
 DR PRINTS: PR01452; NOTCH.  
 DR SMART: SM00248; ANK; 5.  
 DR SMART: SM00179; EGF\_Ca; 23.  
 DR SMART: SM00001; EGF\_like; 11.  
 DR SMART: SM00004; NL; 2.  
 DR PROSITE: PS50088; ANK\_REPEAT; 4.

DR PROSITE: PS50297; ANK\_REPEAT\_REGION; 1.  
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 DR PROSITE: PS00022; EGF\_1; 34.  
 DR PROSITE: PS01186; EGF\_2; 29.  
 DR PROSITE: PS01187; EGF\_Ca; 21.  
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 KW Transmembrane; Signal; Glycoprotein.  
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FT	DISULFID	1084	1093	BY SIMILARITY.
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FT	DISULFID	1115	1130	BY SIMILARITY.
FT	DISULFID	1132	1141	BY SIMILARITY.
FT	DISULFID	1148	1159	BY SIMILARITY.
FT	DISULFID	1168		BY SIMILARITY.

Matches 9; Conservative 3; Mismatches 10; Indels 0; Gaps 0;

Query 6 OKCFQHLDDCCSXKXNXXNCV 27  
 Db 251 ONCEENIDDCPSNCRNGTCV 272

RESULT 4  
 CXOC\_CONCT STANDARD; PRT; 26 AA.  
 AC PS8919;  
 DT 15-JUN-2002 (Rel. 41, Created)  
 DT 15-JUN-2002 (Rel. 41, Last sequence update)  
 DE Omega-conotoxin CVCIC.  
 OS Conus catus (Cat cone).  
 OC Eukaryota; Metazoa; Mollusca; Gastropoda; Caenogastropoda;  
 OC Neogastropoda; Conoidea; Conidae; Conus.  
 OX NCBI\_TaxID=101291;  
 RN [1]  
 RP SEQUENCE, AND SYNTHESIS.  
 RC TISSUE=Venom;  
 RX PubMed=10938268;  
 RA Lewis R.J., Nielsen K.J., Craik D.J., Loughnan M.L., Adams D.A.,  
 RA Sharpe I.A., Luchian T., Adams D.J., Bond T., Thomas L., Jones A.,  
 RA Matheson J.-L., Drinkwater R., Andrews P.R., Alewood P.F.;  
 RT "Novel omega-conotoxins from Conus catus discriminate among neuronal  
 calcium channel subtypes";  
 RL J. Biol. Chem. 275:35335-35344(2000).  
 CC -I- FUNCTION: Omega-conotoxins act at presynaptic membranes, they bind  
 and block voltage-sensitive calcium channels (VSCC) (By  
 similarity). This toxin blocks N-, P-, and Q-type calcium  
 channels.  
 CC -I- SUBCELLULAR LOCATION: Secreted.  
 CC -I- TISSUE SPECIFICITY: Expressed by the venom duct.  
 CC -I- SIMILARITY: BELONGS TO THE O-SUPERFAMILY OF CONOTOXINS. OMEGA-TYPE  
 FAMILY.  
 CC KW Presynaptic neurotoxin; Neurotoxin; Toxin; Calcium channel inhibitor;  
 KW Amidation.  
 FT DISULFID 1 16 BY SIMILARITY.  
 FT DISULFID 8 20 BY SIMILARITY.  
 FT DISULFID 15 26 BY SIMILARITY.  
 FT MOD\_RES 26 26 AMIDATION.  
 SQ SEQUENCE 26 AA; 2790 MW; 56EFC382335C4A8B CRC64;

Query Match Best Local Similarity 39.3%; Score 55; DB 1; Length 26; Pred. No. 0.094; Mismatches 8; Conservative 5; Mismatches 13; Indels 0; Gaps 0;

Query 1 CRXNOKCFQHLDDCCSXKXNXXNC 26  
 Db 1 CKKGQSCSKIMYDCCTGSCSRGKC 26

RESULT 5  
 NOTC\_DROME STANDARD; PRT; 2703 AA.  
 AC P07207; P04154; O97458; O9W4T8;  
 DT 01-NOV-1986 (Rel. 03, Created)  
 DT 15-JUN-2002 (Rel. 41, Last sequence update)  
 DT 15-JUN-2002 (Rel. 41, Last annotation update)  
 DE Neurogenic locus Notch protein precursor.  
 GN N OR EG:140611.1 OR EG:163A10.2 OR CG93936.  
 OS Drosophila melanogaster (Fruit fly).  
 OC Eukaryota; Metazoa; Arthropoda; Mandibulata; Pancrustacea; Hexapoda;  
 OC Insecta; Preygota; Neoptera; Endopterygota; Diptera; Brachycera;  
 OC Muscomorpha; Epiphytoidae; Drosophilidae; Drosophila.  
 OX NCBI\_TaxID=7227;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RC STRAIN=Oregon-R; TISSUE=Embryo;  
 RX MEDLINE=86079539; PubMed=3935325;  
 RA Wharton K.A., Johansen K.M., Xu T., Artavanis-Tsakonas S.;

RT "Nucleotide sequence from the neurogenic locus notch implies a gene  
RT product that shares homology with proteins containing EGF-like  
RT repeats.";  
RL Cell 43:567-581(1985).  
RN [2]  
RP SEQUENCE FROM N.A.  
RC STRAIN-Canton-S, and Oregon-R: TISSUE-Embryo;  
RX MEDLINE=87064624; PubMed=3097517;  
RA Kidd S., Kelley M.R., Young M.W.;  
RT "Sequence of the notch locus of Drosophila melanogaster: relationship  
RT of the encoded protein to mammalian clotting and growth factors.";  
RL Mol. Cell. Biol. 6:3094-3108(1986).  
RN [3]  
RP SEQUENCE FROM N.A.  
RC STRAIN-Berkley;  
RX MEDLINE=20196006; PubMed=10731132;  
RA Adams M.D., Celniker S.E., Holt R.A., Evans C.A., Gocayne J.D.,  
RA Amanatides P.G., Scherer S.E., Li P.W., Hoskins R.A., Galle R.F.,  
RA George R.A., Lewis S.E., Richards S., Ashburner M., Henderson S.N.,  
RA Sutton G.G., Mortman J.R., Yandell M.D., Zhang Q., Chen L.X.,  
RA Brandon R.C., Rogers Y.-H.C., Blazer R.G., Champe M., Pfeiffer B.D.,  
RA Wan K.H., Doyle C., Baxter E.G., Helt G., Nelson C.R., Miklos G.L.G.,  
RA Abrell J.F., Agbayani A., An H.-J., Andrews-Pfannkoch C., Baldwin D.,  
RA Ballew R.M., Basu A., Baxendale J., Bayraktaroglu L., Beasley E.M.,  
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RA Borzova D., Botchan M.R., Bouck J., Brokstein P., Broctier P.,  
RA Burks K.C., Busan D.A., Butler H., Cadieu E., Center A., Chandra I.,  
RA Cherry J.M., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,  
RA de Pablos B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,  
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RA Kimmel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lai Z.,  
RA Lasko P., Lei Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,  
RA Liu X., Matel B., McIntosh T.C., McLeod M.P., McPherson D.,  
RA Merkulov G., Mlshina N.V., Moberly C., Morris J., Moshrefi A.,  
RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,  
RA Nelson D.R., Nelson K.A., Nixon S., Nusskern D.R., Pauley J.M.,  
RA Palazolo M., Pittman G.S., Pan S., Pollard J., Puri V., Reese M.G.,  
RA Reinert K., Remington K., Saunders R.D.C., Scheeler F., Shen H.,  
RA Shue B.C., Siden-Klamos I., Stapleton M., Strong R., Sun E.,  
RA Spier E., Spindling A.C., Stapleton M., Strong R., Sun E.,  
RA Svitzkas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,  
RA Wang Z.-Y., Massarman D.A., Weinstein G.M., Weissbach J.,  
RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,  
RA Ye J., Yeh R.-F., Zaveri J.S., Zhan M., Zhang X., Zhao Q., Zheng L.,  
RA Zheng X.H., Zhong F.N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,  
RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.;  
RT "The genome sequence of Drosophila melanogaster.";  
RL Science 287:2185-2195(2000).  
RN [4]  
RP SEQUENCE FROM N.A.  
RC STRAIN-Oregon R;  
RX MEDLINE=20196011; PubMed=10731137;  
RA Benos P.V., Galt M.K., Ashburner M., Murphy L., Harris D.,  
RA Barrall B.G., Ferraz C., Vidal S., Brun C., Demallies F., Cadieu E.,  
RA Drenth S., Gloux S., Lelaure V., Mottier S., Galibert F., Borzova D.,  
RA Minana B., Kafatos F.C., Louis C., Siden-Klamos I., Bolshakov S.,  
RA Papagiannakis G., Spanos L., Cox S., Madeno E., de Pablos B.,  
RA Modellell J., Peter A., Schoettler P., Werner M., Mourikio F.,  
RA Belnert N., Dowe G., Schaefer U., Jaekle H., Bucheton A.,  
RA Callister D.M., Campbell L.A., Darlamitsou A., Henderson N.S.,  
RA McMillan P.J., Salles C., Tait E.A., Valentini P., Saunders R.D.C.,  
RA Glover D.M.;  
RT "From sequence to chromosome: the tip of the X chromosome of D.  
RT melanogaster.";  
RL Science 287:2220-2222(2000).  
RN [5]  
RP SEQUENCE OF 2505-2611 FROM N.A.  
RX MEDLINE=85099329; PubMed=2981631;  
RA Wharton K.A., Yevonich B., Finerty V.G., Artavanis-Tsakonas S.;  
RT "opa: a novel family of transcribed repeats shared by the Notch locus  
RT and other developmentally regulated loci in D. melanogaster.";  
RL Cell 40:55-62(1985).  
RN [6]  
RP SEQUENCE OF 1-8 FROM N.A.  
RX MEDLINE=87257846; PubMed=3037327;  
RA Kelley M.R., Kidd S., Berg R.L., Young M.W.;  
RT "Restriction of P-element insertions at the Notch locus of Drosophila  
RT melanogaster.";  
RL Mol. Cell. Biol. 7:1545-1548(1987).  
RN [7]  
RP REVIEW  
RA Harris W.A.;  
RT "Many cell types specified by Notch function.";  
RL Curr. Biol. 1:120-122(1991).  
CC -1- FUNCTION: Functions as a receptor for membrane-bound ligands Delta  
CC and Serrate to regulate cell-fate determination. Upon ligand  
CC activation through the released notch intracellular domain (NICD)  
CC it forms a transcriptional activator complex with Su(H)  
CC (Suppressor of hairless) and activates genes of the enhancer of  
CC split locus. Essential for proper differentiation of ectoderm.  
CC -1- SUBCELLULAR LOCATION: Type I membrane protein.  
CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
CC -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
CC -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
CC -1- SIMILARITY: CONTAINS 6 ANK REPEATS.  
CC -----  
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CC -----  
DR EMBL; M16152; AAB59220.1; JOINED.  
DR EMBL; M16153; AAB59220.1; JOINED.  
DR EMBL; M16149; AAB59220.1; JOINED.  
DR EMBL; M16150; AAB59220.1; JOINED.  
DR EMBL; M16151; AAB59220.1; JOINED.  
DR EMBL; K03508; AAA28725.1; JOINED.  
DR EMBL; M13689; AAA28725.1; JOINED.  
DR EMBL; K03507; AAA28725.1; JOINED.  
DR EMBL; AE003426; AAF45848.2; -  
DR EMBL; AL035436; CAB37610.1; -  
DR EMBL; M12175; AAA74496.1; -  
DR EMBL; M16025; AAA28726.1; -  
DR PIR; A24420; A24420.  
DR PIR; A24768; A24768.  
DR PIR; A05267; A05267.  
DR HSSP; P00740; 1EDM.  
DR FLYBASE; FBgn0004647; N.  
DR InterPro; IPR002110; ANK.  
DR InterPro; IPR000152; Asx\_hydroxyl.  
DR InterPro; IPR000561; EGF-like.  
DR InterPro; IPR000742; EGF 2.  
DR InterPro; IPR001881; EGF 2.  
DR InterPro; IPR001438; EGF-11.  
DR InterPro; IPR002049; Laminin\_EGF.  
DR InterPro; IPR000800; Notch.  
DR Pfam; PF00008; EGF; 36.  
DR Pfam; PF00023; ank; 6.  
DR Pfam; PF00066; notch; 3.  
DR PRINTS; PR00010; EGFBL00D.  
DR PRINTS; PR00011; EGF\_LAMININ.  
DR PRINTS; PR01452; NOTCH.  
DR SMART; SM00248; ANK; 7.  
DR SMART; SM00181; EGF; 36.  
DR SMART; SM00179; EGF\_CA; 35.  
DR SMART; SM00004; NL; 2.







FT REPEAT 1168 1208 LIN/NOTCH 1.  
 FT REPEAT 1209 1242 LIN/NOTCH 2.  
 FT REPEAT 1243 1282 LIN/NOTCH 3.  
 FT REPEAT 1628 1657 ANK 1.  
 FT REPEAT 1661 1691 ANK 2.  
 FT REPEAT 1695 1724 ANK 3.  
 FT REPEAT 1728 1757 ANK 4.  
  
 Query Match 37.1%; Score 52; DB 1; Length 1964;  
 Best Local Similarity 35.0%; Pred. No. 7.9;  
 Matches 7; Conservative 5; Mismatches 8; Indels 0; Gaps 0;

QY 8 CFEHLDDCCSXXCNXNKCXV 27  
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 Db 349 CERNLDDCAATCAFGSTCI 368

RESULT 8  
 NTCL\_BRARE STANDARD; PRT; 2437 AA.  
 AC P46530;  
 DT 01-NOV-1995 (Rel. 32, Last sequence update)  
 DT 01-NOV-1995 (Rel. 32, Last sequence update)  
 DT 15-JUN-2002 (Rel. 41, Last annotation update)  
 DE Neurogenic locus notch homolog protein 1 precursor.  
 GN NOTCH1 OR NOTCH.  
 OS Brachydanio rerio (Zebrafish) (Danio rerio).  
 OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;  
 OC Cyprinidae; Danio.  
 RN NCBI\_TaxID=7955;  
 RX SEQUENCE FROM N.A.  
 RC TISSUE=Embryo;  
 RA MEDLINE-94128602; PubMed-8297791;  
 RA Bickkamp C., Campos-Ortega J.A.;  
 RA "A zebrafish homologue of the Drosophila neurogenic gene Notch and  
 RA its pattern of transcription during early embryogenesis.";  
 RL Mech. Dev. 43:87-100(1993).  
 CC -1- FUNCTION: IMPLICATED IN CELL FATE SPECIFICATIONS DURING  
 CC EMBRYO DEVELOPMENT. MAY BE INVOLVED IN THE FORMATION OF THE  
 CC NOTCH PLATE, NOTOCHORD AND BRAIN VESTICLES.  
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein.  
 CC -1- DEVELOPMENTAL STAGE: Expressed in all cells in pregastrulation  
 CC stages. During gastrulation is differentially expressed,  
 CC accumulating predominantly in the prechordal mesoderm and  
 CC notochord. At the end of gastrulation, expressed along the  
 CC anterior-posterior axis including the developing neural plate  
 CC and differentiating mesoderm. Also present in the developing  
 CC brain and head regions.  
 CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 CC -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 6 ANK REPEATS.  
 CC -1- SIMILARITY: CONTAINS 6 ANK REPEATS.  
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 CC -----  
 DR EMBL: X65088; CAA4831.1; -;  
 DR HSP: P00740; 1EDM;  
 DR ZFIN: ZDR-GENE-990415-173; notch1a.  
 DR InterPro: IPR002110; ANK.  
 DR InterPro: IPR000152; Asx\_hydroxyl.  
 DR InterPro: IPR000561; EGF\_1like.  
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 DR InterPro: IPR001881; EGF\_Ca.  
 DR InterPro: IPR001438; EGF\_LI.  
 DR InterPro: IPR000800; Notch.

DR Pfam: PF00008; EGF; 36.  
 DR Pfam: PF00023; ank; 6.  
 DR Pfam: PF00066; notch; 3.  
 DR PRINTS: PR00010; EGFLOOD.  
 DR PRINTS: PR01452; NOTCH.  
 DR SMART: SM00248; ANK; 5.  
 DR SMART: SM00179; EGF\_Ca; 19.  
 DR SMART: SM00001; EGF\_1like; 16.  
 DR SMART: SM00004; NL; 3.  
 DR PROSITE: PS50088; ANK\_REPEAT; 4.  
 DR PROSITE: PS50297; ANK\_REPEAT\_REGION; 1.  
 DR PROSITE: PS00010; ASX\_HYDROXYL; 23.  
 DR PROSITE: PS00022; EGF\_1; 34.  
 DR PROSITE: PS01186; EGF\_2; 28.  
 DR PROSITE: PS01187; EGF\_Ca; 22.  
 KW Receptor; Transcription regulation; Activator; Differentiation;  
 KW Developmental protein; Neurogenesis; Repeat; ANK repeat;  
 KW EGF-like domain; Transmembrane; Glycoprotein; Signal.  
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 FT DOMAIN 21 1724  
 FT TRANSMEM 1725 1747  
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 LIN/NOTCH 2.  
 LIN/NOTCH 3.  
 ANK 1.  
 ANK 2.  
 ANK 3.  
 ANK 4.  
 ANK 5.  
 ANK 6.  
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 CLEAVAGE BY FUZIN-LIKE PROTEASE (BY  
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Query Match 37.1%; Score 52; DB 1; Length 2437;
Best Local Similarity 36.8%; Pred. No. 9.5;
Matches 7; Conservative 4; Mismatches 8; Indels 0; Gaps 0;

Qy 8 CF0HDDCCSXCNXXNC 26
Db 331 CSENIIDCASAASHGATC 349

RESULT 9
NTCL_HUMAN
ID NTCL_HUMAN STANDARD; PRT; 2556 AA.
AC P46531;
DF 01-NOV-1995 (Rel. 32, Created)
DT 15-JUN-2002 (Rel. 41, Last sequence update)
DR 15-JUN-2002 (Rel. 41, Last annotation update)
DE Neurogenic locus notch homolog protein 1 precursor (Notch 1) (hnl)
DE (Translocation-associated notch protein TAN-1).
GN NOTCH1 OR TAN1.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Homnidae; Homo.
OX NCBI_TaxID=9606;
RN [1]
RP SEQUENCE FROM N.A.
RC TISSUE=Brain;
RA Mann R.S., Blumweller C.M., Zagouras P.;
RT "Complete human notch 1 (hnl) cDNA sequence."
RL Submitted (SEP-2000) to the EMBL/genbank/DBJ databases.
RN [2]
RP SEQUENCE OF 1-2444 FROM N.A.
RA MEDLINE=91347367; PubMed=1831692;
RA Edlisen L.W., Bird D.C., Soreng A.L., Reynolds T.C.,
RA Smith S.D., Sklar J.;
RT "TAN-1, the human homolog of the Drosophila notch gene, is broken by
RT chromosome translocations in T lymphoblastic neoplasms."
RL Cell 66:645-661(1991).
RN [3]
RP IDENTIFICATION OF LIGANDS.
RA MEDLINE=99180765; PubMed=10079256;
RA Gray G.E., Mann R.S., Mitsiadis E., Henrique D., Carcangiu M.-L.,
RA Banks A., Leiman J., Ward D., Ish-Horowitz D., Artavanis-Tsakonas S.;
RT Am. J. Pathol. 154:785-794(1999).
RL
CC -1- FUNCTION: Functions as a receptor for membrane-bound ligands
CC Jagged1, Jagged2 and Delta to regulate cell-fate determination.
CC Upon ligand activation through the released notch intracellular
CC domain (NTCD) it forms a transcriptional activator complex with
CC RBP-J kappa and activates genes of the enhancer of split locus.
CC Affects the implementation of differentiation, proliferation and
CC apoptotic programs. May be important for normal lymphocyte
CC function. In altered form, may contribute to transformation or
CC progression in some T-cell neoplasms. Involved in the maturation
CC of both CD4+ and CD8+ cells in the thymus (By similarity).
CC -1- SUBUNIT: Heterodimer of a C-terminal fragment N(TW) and a N-
CC terminal fragment N(EC) which are probably linked by disulfide
CC bonds (By similarity).
CC -1- SUBCELLULAR LOCATION: Type I membrane protein. Following
CC proteolytical processing NTCD is translocated to the nucleus (By
CC similarity).
CC -1- TISSUE SPECIFICITY: In fetal tissues most abundant in spleen,
CC brain stem and lung. Also present in most adult tissues where it
CC is found mainly in lymphoid tissues.
CC -1- PTM: Synthesized in the endoplasmic reticulum as an inactive form
CC which is proteolytically cleaved by a furin-like convertase in the
CC trans-golgi network before it reaches the plasma membrane to yield
CC an active, ligand-accessible form. Cleavage results in a C-
CC terminal fragment N(TW) and a N-terminal fragment N(EC). Following
CC ligand binding, it is cleaved by TNF-alpha converting enzyme
CC (TACE) to yield a membrane-associated intermediate fragment called
CC notch extracellular truncation (NEXT). This fragment is then
CC cleaved by presenilin dependent gamma-secretase to release a

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CC notch-derived peptide containing the intracellular domain (NICD)  
 CC from the membrane (By similarity).  
 CC -1- PTM: Phosphorylated (By similarity).  
 CC -1- DISEASE: Notch1 truncation is associated with neoplasia, a T-cell  
 CC acute lymphoblastic leukemia.  
 CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 CC -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
 CC -1- SIMILARITY: CONTAINS 5 ANK REPEATS.  
 CC -----  
 CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
 CC between the Swiss Institute of Bioinformatics and the EMBL Outstation -  
 CC the European Bioinformatics Institute. There are no restrictions on its  
 CC use by non-profit institutions as long as its content is in no way  
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 CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
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 CC EMBL: AF308602; AAC33848.1; -.  
 CC EMBL: M73980; AAA60614.1; -.  
 CC HSSP: P00740; 1EDM.  
 CC Genew: HGNC:7881; NOTCH1.  
 CC MIM: 190198; -.  
 CC InterPro: IPR002110; ANK.  
 CC InterPro: IPR000152; Asx\_hydroxyl.  
 CC InterPro: IPR000561; EGF-1like.  
 CC InterPro: IPR000742; EGF-2.  
 CC InterPro: IPR001881; EGF\_Ca.  
 CC InterPro: IPR001438; EGF\_II.  
 CC InterPro: IPR000800; Notch.  
 CC Pfam: PF00008; EGF; 36.  
 CC Pfam: PF00023; ank; 6.  
 CC Pfam: PF00066; notch; 3.  
 CC SMART: SM00248; ANK; 5.  
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 CC SMART: SM00001; EGF\_1like; 13.  
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 CC PROSITE: PS01187; EGF\_CA; 18.  
 CC Receptor: Transcription regulation; Activator; Differentiation;  
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 FT DISULFID 14702 14735 BY SIMILARITY.  
 FT DISULFID 14735 14768 BY SIMILARITY.  
 FT DISULFID 14768 14801 BY SIMILARITY.  
 FT DISULFID 14801 14

Db 252 QNCEINIDPCGNCKANGACV 273

RESULT 10

DL3\_MOUSE STANDARD: PRT: 589 AA.

AC 088671; 16-OCT-2001 (Rel. 40, Created)

DT 16-OCT-2001 (Rel. 40, Last sequence update)

DT 15-JUN-2002 (Rel. 41, Last annotation update)

DE Delta-like protein 3 precursor (Drosophila Delta homolog 3).

GN DL3

OS Rattus norvegicus (Rat).

OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.

OX NCBI\_TaxID=10116;

RP SEQUENCE FROM N.A.

RA Boulter J., Greenfield A., Weinmaster G.;

RT "Rattus norvegicus mRNA for Delta 3: a putative ligand for Notch.";

RL Submitted (Aug-1998) to the EMBL/Genbank/DBJ databases.

CC -1- FUNCTION: INHIBITS PRIMARY NEUROGENESIS. MAY BE REQUIRED TO DIVERGENT NEURONS ALONG A SPECIFIC DIFFERENTIATION PATHWAY. PLAY A ROLE IN THE FORMATION OF SOMITE BOUNDARIES DURING SEGMENTATION OF THE PARAXIAL MESODERM (BY SIMILARITY).

CC -1- SUBUNIT: CAN BIND AND ACTIVATE NOTCH-1 OR ANOTHER NOTCH RECEPTOR (BY SIMILARITY).

CC -1- SUBCELLULAR LOCATION: Type I membrane protein (By similarity).

CC -1- DOMAIN: THE DSL DOMAIN IS REQUIRED FOR BINDING TO THE NOTCH RECEPTOR.

CC -1- SIMILARITY: CONTAINS 6 EGF-LIKE DOMAINS.

CC -1- SIMILARITY: CONTAINS 1 DSL DOMAIN.

CC -----

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CC -----

DR EMBL: AF084576; AAC33303.1; -

DR HSSP: P00740; 1EDM.

DR InterPro: IPR000561; EGF-like.

DR InterPro: IPR000742; EGF\_2.

DR InterPro: IPR001881; EGF\_Ca.

DR Pfam: PF00008; EGF\_5.

DR SMART: SM00181; EGF: 6.

DR PROSITE: PS00022; EGF\_1; 6.

DR PROSITE: PS01186; EGF\_2; 5.

KW Signal; EGF-like domain; Repeat; Transmembrane; Developmental protein; Differentiation.

KW SIGNAL 1 32

FT CHAIN 33 589 BY SIMILARITY.

FT DOMAIN 33 494 DELTA-LIKE PROTEIN 3.

FT TRANSMEM 495 515 EXTRACELLULAR (POTENTIAL).

FT DOMAIN 516 589 POTENTIAL.

FT DOMAIN 516 589 CYTOPLASMIC (POTENTIAL).

FT DOMAIN 218 251 DSL.

FT DOMAIN 276 312 EGF-LIKE 1.

FT DOMAIN 314 353 EGF-LIKE 2.

FT DOMAIN 355 391 EGF-LIKE 3.

FT DOMAIN 393 429 EGF-LIKE 4.

FT DOMAIN 431 467 EGF-LIKE 5.

FT DOMAIN 503 511 EGF-LIKE 6.

FT DOMAIN 511 511 POLY-ALA.

FT DISULFID 222 233 BY SIMILARITY.

FT DISULFID 226 239 BY SIMILARITY.

FT DISULFID 241 250 BY SIMILARITY.

FT DISULFID 280 291 BY SIMILARITY.

FT DISULFID 285 300 BY SIMILARITY.

FT DISULFID 302 311 BY SIMILARITY.

FT DISULFID 318 329 BY SIMILARITY.

FT DISULFID 323 341 BY SIMILARITY.

Query Match 36.4%; Score 51; DB 1; Length 589;

Best Local Similarity 34.5%; Pred. No. 4.1;

Matches 10; Conservative 1; Mismatches 16; Indels 2; Gaps 1;

QY 1 CR-1XNOKCFHLDCCSXCKNXXKCV 27

Db 381 CRAGFAGRCHEHDDCAGACANGCTCV 409

DL3\_MOUSE STANDARD: PRT: 592 AA.

AC 088516; Q9QW27; Q35675; Q9QWL9;

DT 16-OCT-2001 (Rel. 40, Created)

DT 16-OCT-2001 (Rel. 40, Last sequence update)

DT 15-JUN-2002 (Rel. 41, Last annotation update)

DE Delta-like protein 3 precursor (Drosophila Delta homolog 3) (M-Delta-3).

GN DL3

OS Mus musculus (Mouse).

OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;

OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.

OX NCBI\_TaxID=10090;

RP SEQUENCE FROM N.A. (ISOFORM 1).

RC STRAIN=C57BL/6 X DBA; TISSUE=Embryo;

RX MEDLINE=97417575; PubMed=9272948;

RA Dunwoode S.L., Henrique D.M.P., Harrison S.M., Beddington R.S.P.;

RT "Mouse Dll3: a novel divergent Delta gene which may complement the function of other Delta homologues during early pattern formation in the mouse embryo.";

RT Development 124:3065-3076(1997).

RL [2]

RP SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.

RC STRAIN=129/SVJ;

RX MEDLINE=98324780; PubMed=9662403;

RA Kusumi K., Sun E.S., Keirebrock A.W., Bronson R.T., Chi D.-C., Bulotsky M.S., Spencer J.B., Birren B.W., Frankel W.N., Lander E.S.;

RT "The mouse pudgy mutation disrupts Delta homologue Dll3 and initiation of early somite boundaries.";

RT Nat. Genet. 19:274-278(1998).

RL [3]

RP SEQUENCE FROM N.A. (ISOFORM 1).

RC TISSUE=Neural tube;

RA Nakayama K., Nakayama N., Tomooka Y., Hayashi Y., Takahashi M.;

RT "Specific expression of a divergent type of Delta in a set of earliest generated neurons including the prospective subplate neurons.";

RL Submitted (Apr-1998) to the EMBL/Genbank/DBJ databases.

CC -1- FUNCTION: INHIBITS PRIMARY NEUROGENESIS. MAY BE REQUIRED TO DIVERGENT NEURONS ALONG A SPECIFIC DIFFERENTIATION PATHWAY. PLAY A ROLE IN THE FORMATION OF SOMITE BOUNDARIES DURING SEGMENTATION OF THE PARAXIAL MESODERM.

CC -1- SUBUNIT: CAN BIND AND ACTIVATE NOTCH-1 OR ANOTHER NOTCH RECEPTOR (PROBABLY).

CC -1- SUBCELLULAR LOCATION: Type I membrane protein (Probable).

CC -1- ALTERNATIVE PRODUCTS: 2 ISOFORMS: 1 AND 2 (SHOWN HERE); ARE PRODUCED BY ALTERNATIVE SPLICING.

CC -1- TISSUE SPECIFICITY: PREDOMINANTLY EXPRESSED IN THE NEUROECTODERM AND PARAXIAL MESODERM DURING EMBRYOGENESIS.

CC -1- DOMAIN: THE DSL DOMAIN IS REQUIRED FOR BINDING TO THE NOTCH RECEPTOR.

```

-1- DISEASE: A TRUNCATING MUTATION IN DL3 IS THE CAUSE OF THE PUDGY
(CC) (PD) PHENOTYPE. PUDGY MICE EXHIBIT PATTERNING DEFECTS AT THE
(CC) EARLIEST STAGES OF SOMITOGENESIS. ADULT PUDGY MICE PRESENT SEVERE
(CC) VERTICAL AND RIB DEFORMITIES.
(CC) -1- SIMILARITY: CONTAINS 6 EGF-LIKE DOMAINS.
(CC) -1- SIMILARITY: CONTAINS 1 DSL DOMAIN.
-----
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DR EMBL: AF068865; AAC40170.1; -
DR EMBL: AF068865; AAC40169.1; -
DR EMBL: Y11895; CAAT2637.1; -
DR EMBL: AB013440; BAA33716.1; -
DR HSSP: P00740; IEDM.
DR MGD: MGI:1096877; D113.
DR InterPro: IPR000561; EGF-like.
DR InterPro: IPR000742; EGF_2.
DR InterPro: IPR001881; EGF_Ca.
DR InterPro: IPR001438; EGF_11.
DR Pfam: PF00008; EGF; 5.
DR PRINTS: PR00010; EGFBLOOD.
DR SMART: SMO0181; EGF; 6.
DR PROSITE: PS00022; EGF_1; 6.
DR PROSITE: PS01186; EGF_2; 6.
KW Signal; EGF-like domain; Repeat; Transmembrane; Developmental protein;
KW Differential; Alternative splicing.
FT SIGNAL 1 32
FT CHAIN 33 592
FT DOMAIN 33 490 DELTA-LIKE PROTEIN 3.
FT TRANSMEM 491 511 EXTRACELLULAR (POTENTIAL).
FT DOMAIN 512 592 POTENTIAL.
FT DOMAIN 174 213 CYTOPLASMIC (POTENTIAL).
FT DOMAIN 214 247 DSL.
FT DOMAIN 272 308 EGF-LIKE 1.
FT DOMAIN 310 349 EGF-LIKE 2.
FT DOMAIN 351 387 EGF-LIKE 3.
FT DOMAIN 389 425 EGF-LIKE 4.
FT DOMAIN 427 463 EGF-LIKE 5.
FT DOMAIN 463 529 EGF-LIKE 6.
FT DISULFID 218 229 BY SIMILARITY.
FT DISULFID 222 235 BY SIMILARITY.
FT DISULFID 237 246 BY SIMILARITY.
FT DISULFID 276 287 BY SIMILARITY.
FT DISULFID 281 296 BY SIMILARITY.
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FT DISULFID 398 413 BY SIMILARITY.
FT DISULFID 415 424 BY SIMILARITY.
FT DISULFID 431 442 BY SIMILARITY.
FT DISULFID 436 451 BY SIMILARITY.
FT DISULFID 453 462 BY SIMILARITY.
FT VASPLC 585 592 DMLQVLE -> A (IN ISOFORM 1).
FT CONFLICT 94 94 E -> K (IN REF. 3).
FT CONFLICT 401 401 G -> A (IN REF. 1).
SQ SEQUENCE 592 AA; 62069 MW; 1A84F8022E7EDCC CRC64;

Query Match 36.4%; Score 51; DB 1; Length 592;
Best Local Similarity 34.5%; Pred. No. 4.1;
Matches 10; Conservative 1; Mismatches 16; Indels 2; Gaps 1;

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DB 377 CRAGFAGRCHEHDDDCAGRACANGCTCV 405

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RESULT 12
DLI3_HUMAN
ID DLI3_HUMAN STANDARD; PRT; 618 AA.
AC Q9NYJ7;
DT 16-OCT-2001 (Rel. 40, Created)
DT 16-OCT-2001 (Rel. 40, Last sequence update)
DT 15-JUN-2002 (Rel. 41, Last annotation update)
DE Delta-like protein 3 precursor (Drosophila Delta homolog 3).
GN DLI3.
OS Homo sapiens (Human).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Primates; Catarrhini; Hominiidae; Homo.
OX NCBI_TaxID=9606;
PI
[1]
SEQUENCE FROM N.A., AND VARIANT SD ASP-385.
RX MEDLINE=2020573; PubMed=10742114;
RA Butler M.P., Kusumi K., Fraying T.M., McKewen C., Garrett C.,
RA Lander E.S., Krumlauf R., Hatterley A.T., Ellard S., Turney P.D.;
RT "Mutations in the human delta homologue, DLI3, cause axial skeletal
RT defects in spondylocostal dysostosis."
RL Nat. genet. 24:438-441(2000).
RN [2]
RP SEQUENCE FROM N.A.
RC TISSUE=Brain;
RA Strausberg R.;
RL Submitted (NOV-2000) to the EMBL/GenBank/DDBJ databases.
CC -1- FUNCTION: INHIBITS PRIMARY NEUROGENESIS. MAY BE REQUIRED TO DIVERT
CC NEURONS ALONG A SPECIFIC DIFFERENTIATION PATHWAY. PLAY A ROLE IN
CC THE FORMATION OF SOMITE BOUNDARIES DURING SEGMENTATION OF THE
CC PARAXIAL MESODERM (BY SIMILARITY).
CC -1- SUBUNIT: CAN BIND AND ACTIVATE NOTCH-1 OR ANOTHER NOTCH RECEPTOR
CC (BY SIMILARITY).
CC -1- SUBCELLULAR LOCATION: Type I membrane protein (Probable).
CC -1- DOMAIN: THE DSL DOMAIN IS REQUIRED FOR BINDING TO THE NOTCH
CC RECEPTOR.
CC -1- DISEASE: DEFECTS IN DLI3 ARE A CAUSE OF AUTOSOMAL RECESSIVE
CC SPONDYLOCOSTAL DYSOSTOSIS (SD). IT IS CHARACTERIZED BY MULTIPLE
CC HEMIVERTEBRAE, RIB FUSIONS AND DELETIONS WITH A NON-PROGRESSIVE
CC KYPHOSCOLIOSIS.
CC -1- SIMILARITY: CONTAINS 6 EGF-LIKE DOMAINS.
CC -1- SIMILARITY: CONTAINS 1 DSL DOMAIN.
CC -----
CC This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC use by non-profit institutions as long as its content is in no way
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CC -----
DR EMBL; AF241373; AAF62542.1; -
DR EMBL; AF241367; AAF62542.1; JOINED.
DR EMBL; AF241368; AAF62542.1; JOINED.
DR EMBL; AF241369; AAF62542.1; JOINED.
DR EMBL; AF241370; AAF62542.1; JOINED.
DR EMBL; AF241371; AAF62542.1; JOINED.
DR EMBL; AF241372; AAF62542.1; JOINED.
DR EMBL; BC000218; AAH00218.1; -
DR HSSP; P00740; IEDM.
DR HSPG; HGNC:2909; DLI3.
DR MIM; 602768; -.
DR MIM; 277300; -.
DR InterPro; IPR000561; EGF-like.
DR InterPro; IPR000742; EGF_2.
DR InterPro; IPR001881; EGF_Ca.
DR InterPro; IPR001438; EGF_II.
DR Pfam; PF00008; EGF_5.
DR PRINTS; PRO010; EGFBLDOD.
DR SMART; SM00181; EGF_6.
DR PROSITE; PS00022; EGF_1; 6.
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DR PROSITE: PS01186; EGF\_2; 6.  
 KW Signal; EGF-like domain; Repeat; Transmembrane; Developmental protein;  
 KM Differentiation; Disease mutation.  
 FT SIGNAL 1 26  
 FT CHAIN 27 618  
 FT DOMAIN 27 492  
 FT TRANSSEM 493 513  
 FT DOMAIN 514 618  
 FT DOMAIN 176 215  
 FT DOMAIN 216 249  
 FT DOMAIN 274 310  
 FT DOMAIN 312 351  
 FT DOMAIN 353 389  
 FT DOMAIN 391 427  
 FT DOMAIN 429 465  
 FT DISULFID 220 231  
 FT DISULFID 224 237  
 FT DISULFID 239 248  
 FT DISULFID 278 289  
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 FT DISULFID 362 377  
 FT DISULFID 379 388  
 FT DISULFID 395 406  
 FT DISULFID 400 415  
 FT DISULFID 417 426  
 FT DISULFID 433 444  
 FT DISULFID 438 453  
 FT DISULFID 455 464  
 FT VARIANT 385  
 FT  
 SQ SEQUENCE 618 AA; 64617 MW; 58AB9CA7DEAD1A0 CRC64;  
 Query Match 36.4%; Score 51; DB 1; Length 618;  
 Best Local Similarity 34.5%; Pred. No. 4.3;  
 Matches 10; Conservative 1; Mismatches 16; Indels 2; Gaps 1;  
 QY 1 CR--IXNKKCFQHLDDCCSXNXXNVCV 27  
 Db 379 CRAFGAPRCEHDLDDCAGRACANGGCV 407  
 RESULT 13  
 NTC4\_HUMAN STANDARD; PRT: 2003 AA.  
 AC 099466; 000306; 099940; 099458; 099358; 090119; 090110;  
 DT 15-JUN-2002 (Rel. 41, Created)  
 DT 15-JUN-2002 (Rel. 41, Last annotation update)  
 DE Neogenetic locus notch homolog protein 4 precursor (Notch 4)  
 DE (hntch4).  
 GN NOTCH4.  
 OS Homo sapiens (Human).  
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Primates; Catarrhini; Homiidae; Homo.  
 OX NCBI\_TaxID=9606;  
 RN (1)  
 RP SEQUENCE FROM N.A. (ISOFORM 1), AND POLYMORPHISM OF POLY-LEU.  
 RC TISSUE=Placenta;  
 RX MEDLINE=97311416; PubMed=9168133;  
 RA Sugaya K., Sasahuma S.-I., Nohata J., Kimura T., Fukagawa T.,  
 RA Nakamura Y., Ando A., Inoko H., Ikemura T., Mita K.;  
 RT "Gene organization of human NOTCH4 and (CTG)n polymorphism in this  
 human counterpart gene of mouse proto-oncogene Int3.";  
 RL Gene 189:235-244(1997).  
 RN (2)  
 RP SEQUENCE FROM N.A. (ISOFORMS 1; 2 AND 3).  
 RC TISSUE=Bone marrow, and Heart;  
 RX MEDLINE=98360091; PubMed=9693032;

RA Li L., Huang G.M., Banta A.B., Deng Y., Smith T., Dong P.,  
 RA Friedman C., Chen L., Trask B.J., Spies T., Rowen L., Hood L.;  
 RT "Cloning, characterization, and the complete 56.8-kilobase DNA  
 RT sequence of the human NOTCH4 gene.";  
 RN Genomics 51:45-58(1998).  
 RP SEQUENCE OF 1-503 FROM N.A., AND VARIANTS GLN-117 AND GLN-317.  
 RA Miyagawa T., Tokunaga K., Hojho H.;  
 RT "Human notch4 gene variant.";  
 RN Submitted (FEB-1999) to the EMBL/Genbank/DBJ databases.  
 RP IDENTIFICATION OF LIGANDS.  
 RX MEDLINE=99180765; PubMed=10079256;  
 RA Gray G.E., Mann R.S., Mitsiadis E., Henrique D., Carcangiu M.-L.,  
 RA Banks A., Leiman J., Ward D., Ish-Horowitz D., Aravanis-Tsakonas S.,  
 RL Am. J. Pathol. 154:785-794(1999).  
 CC -1- FUNCTION: Functions as a receptor for membrane-bound ligands  
 CC jagged1, jagged2 and deltal to regulate cell-fate determination.  
 CC Upon ligand activation through the released notch intracellular  
 CC domain (NICD) it forms a transcriptional activator complex with  
 CC RBP-J kappa and activates genes of the enhancer of split locus.  
 CC Affects the implementation of differentiation, proliferation and  
 CC apoptotic programs. May regulate branching morphogenesis in the  
 CC developing vascular system (By similarity).  
 CC -1- SUBUNIT: Heterodimer of a C-terminal fragment N(TM) and a N-  
 CC terminal fragment N(TEC) which are probably linked by disulfide  
 CC bonds (By similarity).  
 CC -1- SUBCELLULAR LOCATION: Type I membrane protein. Following  
 CC proteolytical processing NICD is translocated to the nucleus.  
 CC -1- ALTERNATIVE PRODUCTS: 3 isoforms; 1 (shown here), 2 and 3; may be  
 CC produced by alternative splicing.  
 CC -1- TISSUE SPECIFICITY: Highly expressed in the heart, skeletal  
 CC muscle, kidney, pancreas, spleen, lymph node, thymus, bone marrow  
 CC and fetal liver. No expression was seen in adult brain or  
 CC peripheral blood leukocytes.  
 CC -1- PTM: Synthesized in the endoplasmic reticulum as an inactive form  
 CC which is proteolytically cleaved by a furin-like convertase in the  
 CC trans-golgi network before it reaches the plasma membrane to yield  
 CC an active, ligand-accessible form. Cleavage results in a C-  
 CC terminal fragment N(TM) and a N-terminal fragment N(TEC). Following  
 CC ligand binding, it is cleaved by TNF-alpha converting enzyme  
 CC (TACE) to yield a membrane-associated intermediate fragment called  
 CC notch extracellular truncation (NEXT). This fragment is then  
 CC cleaved by presenilin dependent gamma-secretase to release a  
 CC notch-derived peptide containing the intracellular domain (NICD)  
 CC from the membrane (By similarity).  
 CC -1- PTM: Phosphorylated (By similarity).  
 CC -1- POLYMORPHISM: The poly-leu region of NOTCH4 (in the signal  
 CC peptide) is polymorphic and the number of leu varies in the  
 CC population (from 6 to 12).  
 CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
 CC -1- SIMILARITY: CONTAINS 28 EGF-LIKE DOMAINS.  
 CC -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
 CC -1- CAUTION: Ref.1 sequence differs from that shown due to frameshifts  
 CC in position 1438 to 1463.  
 CC  
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 CC  
 CC EMBL: D63395; BAA09708.1; ALT\_FRAME.  
 CC EMBL: D86566; BAA13116.1; -  
 CC EMBL: U95299; AAC32288.1; -  
 CC EMBL: U89335; AAC63097.1; -  
 CC EMBL: AB023961; BAB20317.1; -  
 CC EMBL: AB024520; BAA88951.1; -

DR EMBL; AB024578; BAA8952.1; -  
 DR HSSP; P08709; 1BF9.  
 DR Genew; HGNC:7884; NOTCH4.  
 DR MIM; 164951; -  
 DR InterPro; IPR002110; ANK.  
 DR InterPro; IPR000152; Asx\_hydroxyl.  
 DR InterPro; IPR000561; EGF-like.  
 DR InterPro; IPR000742; EGF\_2.  
 DR InterPro; IPR001881; EGF\_Ca.  
 DR InterPro; IPR001438; EGF-IT.  
 DR InterPro; IPR000800; Notch.  
 DR Pfam; PF00008; EGF; 26.  
 DR Pfam; PF00023; ank; 6.  
 DR Pfam; PF00066; notch; 2.  
 DR PRINTS; PR00010; EGFBL00.  
 DR PRINTS; PR00011; EGFAMININ.  
 DR PRINTS; PR00012; ENTPEI.  
 DR SMART; SM00248; ANK; 5.  
 DR SMART; SM00179; EGF\_CA; 11.  
 DR SMART; SM00001; EGF-like; 15.  
 DR SMART; SM00004; NL; 2.  
 DR PROSITE; PSS0088; ANK\_REPEAT; 5.  
 DR PROSITE; PSS0297; ANK\_REPEAT\_REGION; 1.  
 DR PROSITE; PSS0010; ASX\_HYDROXYL; 11.  
 DR PROSITE; PSS00022; EGF\_1; 28.  
 DR PROSITE; PSS0186; EGF\_2; 21.  
 DR PROSITE; PSS0187; EGF\_CA; 9.  
 KW Receptor: Transcription regulation; Activator; Differentiation;  
 KW Developmental protein: Repeat: ANK repeat: EGF-like domain;  
 KW Transmembrane; Glycoprotein; Signal; Phosphorylation; Polymorphism;  
 KW Triplet repeat expansion; Alternative splicing.  
 FT SIGNAL 1 23  
 FT CHAIN 24 2003  
 FT CHAIN 1432 2003  
 FT CHAIN 1467 2003  
 FT CHAIN 1467 2003  
 FT TRANSMEM 24 1447  
 FT DOMAIN 1448 1468  
 FT DOMAIN 1469 2003  
 FT DOMAIN 24 63  
 FT DOMAIN 64 115  
 FT DOMAIN 118 155  
 FT DOMAIN 156 192  
 FT DOMAIN 194 232  
 FT DOMAIN 234 274  
 FT DOMAIN 276 312  
 FT DOMAIN 314 353  
 FT DOMAIN 355 391  
 FT DOMAIN 392 430  
 FT DOMAIN 432 473  
 FT DOMAIN 475 511  
 FT DOMAIN 513 549  
 FT DOMAIN 551 587  
 FT DOMAIN 589 625  
 FT DOMAIN 626 659  
 FT DOMAIN 661 689  
 FT DOMAIN 691 727  
 FT DOMAIN 729 765  
 FT DOMAIN 767 803  
 FT DOMAIN 806 842  
 FT DOMAIN 844 880  
 FT DOMAIN 882 928  
 FT DOMAIN 930 966  
 FT DOMAIN 968 1004  
 FT DOMAIN 1006 1044  
 FT DOMAIN 1046 1085  
 FT DOMAIN 1087 1126  
 FT DOMAIN 1130 1171  
 FT DOMAIN 1172 1212  
 FT REPEAT 1165 1212  
 FT REPEAT 1213 1246  
 FT REPEAT 1247 1286

FT REPEAT 1633 1665 ANK 1.  
 FT REPEAT 1666 1698 ANK 2.  
 FT REPEAT 1700 1732 ANK 3.  
 FT REPEAT 1733 1765 ANK 4.  
 FT REPEAT 1766 1798 ANK 5.  
 FT DISULFID 28 41  
 FT DISULFID 35 51  
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 FT DISULFID 105 114  
 FT DISULFID 122 133  
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 FT DISULFID 343 352  
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 Best Local Similarity 35.0%; Pred. No. 11;  
 Matches 7; Conservative 5; Mismatches 8; Indels 0; Gaps 0;  
 QY 8 CPOHLDDCCXXKXNKCXV 27  
 Db 352 CERNLDDCTAATCAPOSTCI 371  
 RESULT 14  
 NC1\_MOUSE  
 AC 001705; Q9QW58; Q99JC2; Q06007; Q61905; Q9R0X7;  
 DT 01-NOV-1995 (Rel. 32, Created)  
 DT 01-FEB-1996 (Rel. 33, Last sequence update)  
 DT 15-JUN-2002 (Rel. 41, Last annotation update)  
 DE Neurogenic locus notch homolog protein 1 precursor (Notch 1) (Notch A)  
 DE (MIM14) (P3800).  
 GN NOTCH1 OR NOTCH.  
 OS Mus musculus (Mouse).  
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
 OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Mus.  
 OX NCBI\_Taxid=10090;  
 RN [1]  
 RP SEQUENCE FROM N.A. (ISOFORM 1).  
 RC TISSUE=Embryo;  
 RA MEDLINE=93194170; PubMed=8449489;  
 RA Franco del Amo F., Gendron-Maguire M., Swiatek P.D., Jenkins N.A.,  
 RA Copeland N.G., Gridley T.;  
 RT "Cloning, analysis, and chromosomal localization of Notch-1, a mouse  
 RT homolog of Drosophila Notch.";  
 RL Genomics 15:259-264(1993).  
 RN [2]  
 RP SEQUENCE OF 731-1899 FROM N.A. (ISOFORM 2), AND DEVELOPMENTAL STAGE.  
 RC STRAIN=CD-1; TISSUE=Embryo;  
 RX MEDLINE=93050801; PubMed=1426644;  
 RX Reaume A.G., Conlon R.A., Ziringib R., Yamaguchi T.P., Rossant J.;  
 RT "Expression analysis of a Notch homologue in the mouse embryo.";  
 RL Dev. Biol. 154:377-387(1992).  
 RN [3]  
 RP SEQUENCE OF 1551-1647 FROM N.A. (ISOFORM 1), AND DEVELOPMENTAL STAGE.  
 RC TISSUE=Embryo;  
 RX MEDLINE=93048835; PubMed=1425352;



RA Franco del Amo F., Smith D.E., Swiatek P.J., Gendron-Maguire M.,  
RA Greenspan R.J., McMahon A.P., Gridley T.;  
RT "Expression pattern of Notch, a mouse homolog of Drosophila Notch,  
RT suggests an important role in early postimplantation mouse  
RT development.";  
RL Development 115:737-744(1992).  
RN [4]  
RP SEQUENCE OF 1161-1547 FROM N.A.  
RX STRAIN=C57BL/6 X CBA; TISSUE=Embryo;  
RC MEDLINE=93178563; PubMed=8440332;  
RA Lardelli M., Lendahl U.;  
RT "Notch A and Notch B-two mouse Notch homologues coexpressed in a  
RT wide variety of tissues";  
RL Exp. Cell Res. 204:364-372(1993).  
RN [5]  
RP SEQUENCE OF 1659-1673 FROM N.A.  
RX MEDLINE=99364499; PubMed=10437788;  
RA Lee J.S., Ishimoto A., Yanagawa S.I.;  
RT "Murine leukemia provirus-mediated activation of the Notch1 gene leads  
RT to induction of HES-1 in a mouse T lymphoma cell line, DL-3.";  
RL FEBS Lett. 455:276-280(1999).  
RN [6]  
RP SEQUENCE OF 1950-2201 FROM N.A.  
RX MEDLINE=98029496; PubMed=9384671;  
RA Messier M., Pollo M., Nehls M., Eggert H., Boehm T.;  
RT "Dynamic changes in gene expression during in vitro differentiation of  
RT mouse embryonic stem cells.";  
RL Cytokines Cell. Mol. Ther. 1:139-143(1995).  
RN [7]  
RP SEQUENCE OF 1655-1659, CLEAVAGE BY FURIN-LIKE CONVERTASE, AND  
RX NOTAGENSIS OF 1651-ARG-GLN-ARG-ARG-1654.  
RA MEDLINE=98318619; PubMed=9653148;  
RX Logeat F., Bessia C., Brou C., Lebail O., Jarriault S., Seidah N.G.,  
RA Israel A.;  
RT "The Notch1 receptor is cleaved constitutively by a furin-like  
RT convertase.";  
RL Proc. Natl. Acad. Sci. U.S.A. 95:8108-8112(1998).  
RN [8]  
RP PARTIAL SEQUENCE, AND POST-TRANSLATIONAL PROCESSING.  
RX MEDLINE=21523956; PubMed=11518718;  
RA Saxena M.T., Schroeter E.H., Mumm J.S., Kopan R.;  
RT "Murine notch homologs (NL-4) undergo presenilin-dependent  
RT proteolysis.";  
RL J. Biol. Chem. 276:40268-40273(2001).  
RN [9]  
RP POST-TRANSLATIONAL PROCESSING.  
RX MEDLINE=21374376; PubMed=11459941;  
RA Mizutani T., Taniguchi Y., Aoki T., Hashimoto N., Honjo T.;  
RT "Conservation of the biochemical mechanisms of signal transduction  
RT among mammalian Notch family members.";  
RL Proc. Natl. Acad. Sci. U.S.A. 98:9026-9031(2001).  
RN [10]  
RP -1- FUNCTION: Functions as a receptor for membrane-bound ligands  
CC Jagged1, Jagged2 and Delta to regulate cell-fate determination.  
CC Upon ligand activation through the released notch intracellular  
CC domain (NICD) it forms a transcriptional activator complex with  
CC RBP-J kappa and activates genes of the enhancer of split locus.  
CC Affects the implementation of differentiation, proliferation and  
CC apoptotic programs (By similarity). May play an essential role in  
CC postimplantation development, probably in some aspect of cell  
CC specification and/or differentiation. May be involved in mesoderm  
CC development, somit formation and neurogenesis. Involved in the  
CC maturation of both CD4+ and CD8+ cells in the thymus.  
CC [11]  
RP -1- SUBUNIT: Heterodimer of a C-terminal fragment N(TM) and a N-  
CC terminal fragment N(EC) which are probably linked by disulfide  
CC bonds.  
CC [12]  
RP -1- SUBCELLULAR LOCATION: Type I membrane protein. Following  
CC proteolytical processing NICD is translocated to the nucleus.  
CC [13]  
RP -1- ALTERNATIVE PRODUCTS: 2 isoforms; 1 (shown here) and 2; may be  
CC produced by alternative splicing.  
CC [14]  
RP -1- TISSUE SPECIFICITY: Highly expressed in the brain, lung and  
CC thymus. Expressed at lower levels in the spleen, bone-marrow,  
CC spinal cord, eyes, mammary gland, liver, intestine, skeletal  
CC muscle, kidney and heart.

CC -1- DEVELOPMENTAL STAGE: First detected in the mesoderm at 7.5 d.p.c.  
CC By 8.5 d.p.c. highly expressed in presomitic mesoderm, mesenchyme  
CC and endothelial cells, while much lower levels are seen in the  
CC neuroepithelium. Between 9.5-10.5 d.p.c. expressed at high levels  
CC in the neuroepithelium. At 13.5 d.p.c. expressed in the surface  
CC ectoderm, eye and developing whisker follicles.  
CC [15]  
RP -1- PTM: Synthesized in the endoplasmic reticulum as an inactive form  
CC which is proteolytically cleaved by a furin-like convertase in the  
CC trans-Golgi network before it reaches the plasma membrane to yield  
CC an active, ligand-accessible form. Cleavage results in a C-  
CC terminal fragment N(TM) and a N-terminal fragment N(EC). Following  
CC ligand binding, it is cleaved by TNF-alpha converting enzyme  
CC (TACE) to yield a membrane-associated intermediate fragment called  
CC notch extracellular truncation (NEXT). This fragment is then  
CC cleaved by presenilin dependent gamma-secretase to release a  
CC notch-derived peptide containing the intracellular domain (NICD)  
CC from the membrane.  
CC [16]  
RP -1- PTM: Phosphorylated.  
CC [17]  
RP -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.  
CC [18]  
RP -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.  
CC [19]  
RP -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.  
CC [20]  
RP -1- SIMILARITY: CONTAINS 5 ANK REPEATS.  
CC [21]  
RP -----  
CC This SWISS-PROT entry is copyright. It is produced through a collaboration  
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CC or send an email to [license@isb-sib.ch](mailto:license@isb-sib.ch)).  
CC -----  
CC EMBL: Z11886; CAA77941.1; -  
CC EMBL: L02613; AAK1498.1; -  
CC EMBL: X68278; CAA48339.1; -  
CC EMBL: AJ238029; CAA40733.1; -  
CC EMBL: X82562; CAA57909.1; -  
CC HSSP: P00740; IEDM.  
CC MGD: MGI:97363; Notch1.  
CC InterPro: IPR002110; ANK.  
CC InterPro: IPR000152; Asx\_hydroxyl.  
CC InterPro: IPR000561; EGF-like.  
CC InterPro: IPR007442; EGF\_2.  
CC InterPro: IPR001881; EGF\_CA.  
CC InterPro: IPR001438; EGF\_11.  
CC InterPro: IPR000800; Notch.  
CC Pfam: PF00008; EGF; 35.  
CC Pfam: PF00023; ank; 7.  
CC Pfam: PF00066; notch; 3.  
CC PRINTS: PR00010; EGFBLDOD.  
CC PRINTS: PR01452; NOTCH.  
CC SMART: SM00248; ANK; 3.  
CC SMART: SM00179; EGF\_CA; 23.  
CC SMART: SM00001; EGF-like; 11.  
CC SMART: SM00004; NL; 2.  
CC PROSITE: PS50088; ANK\_REPEAT; 2.  
CC PROSITE: PS50297; ANK\_REPEAT\_REGION; 1.  
CC PROSITE: PS00010; ASX\_HYDROXYL; 22.  
CC PROSITE: PS00022; EGF\_1; 34.  
CC PROSITE: PS01186; EGF\_2; 27.  
CC PROSITE: PS01187; EGF\_CA; 21.  
CC Receptor; Transcription regulation; Activator; Differentiation;  
CC Developmental protein; Repeat; ANK repeat; EGF-like domain;  
CC Transmembrane; Glycoprotein; Signal; Phosphorylation;  
CC Alternative splicing.  
CC SIGNAL 18  
CC CHAIN 19 2531 POTENTIAL.  
CC CHAIN 1711 2531 NEUROGENIC LOCUS NOTCH HOMOLOG PROTEIN 1.  
CC CHAIN 1744 2531 NOTCH EXTRACELLULAR TRUNCATION.  
CC CHAIN 1744 2531 NOTCH INTRACELLULAR DOMAIN.  
CC CHAIN 1725 1725 EXTRACELLULAR (POTENTIAL).  
CC TRANSMEM 1726 1746 POTENTIAL.  
CC DOMAIN 1747 2531 CYTOPLASMIC (POTENTIAL).  
CC DOMAIN 20 58 EGF-LIKE 1.  
CC DOMAIN 59 99 EGF-LIKE 2.

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FT DOMAIN 102 139 EGF-LIKE 3.
FT DOMAIN 140 176 EGF-LIKE 4.
FT DOMAIN 178 216 EGF-LIKE 5.
FT DOMAIN 218 255 EGF-LIKE 6.
FT DOMAIN 257 293 EGF-LIKE 7.
FT DOMAIN 295 333 EGF-LIKE 8.
FT DOMAIN 335 371 EGF-LIKE 9.
FT DOMAIN 372 410 EGF-LIKE 10.
FT DOMAIN 412 450 EGF-LIKE 11.
FT DOMAIN 452 488 EGF-LIKE 12.
FT DOMAIN 490 526 EGF-LIKE 13.
FT DOMAIN 528 564 EGF-LIKE 14.
FT DOMAIN 566 601 EGF-LIKE 15.
FT DOMAIN 603 639 EGF-LIKE 16.
FT DOMAIN 641 676 EGF-LIKE 17.
FT DOMAIN 678 714 EGF-LIKE 18.
FT DOMAIN 716 751 EGF-LIKE 19.
FT DOMAIN 753 789 EGF-LIKE 20.
FT DOMAIN 791 827 EGF-LIKE 21.
FT DOMAIN 829 867 EGF-LIKE 22.
FT DOMAIN 869 905 EGF-LIKE 23.
FT DOMAIN 907 943 EGF-LIKE 24.

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Query Match 36.4% Score 51; DB 1; Length 2531;
Best Local Similarity 36.4% Pred. No. 13;
Matches 8; Conservative 3; Mismatches 11; Indels 0; Gaps 0;

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QY 6 QKCFHLDCCSXKXNXCVCV 27
Db 252 QNCEENYDDCGNCKNGACV 273

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RESULT 15
ID NCCL RAT STANDARD; PRT; 2531 AA.
AC 007008:
DT 01-NOV-1995 (Rel. 32, Created)
DT 15-JUL-1999 (Rel. 38, Last sequence update)
DT 15-JUN-2002 (Rel. 41, Last annotation update)
DE Neurogenic locus notch homolog protein 1 precursor (Notch 1).
GN NOTCH1.
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
ON NCCL_TaxID=10116;
OX (1)
RP SEQUENCE FROM N.A.
RC TISSUE-Schwann cell;
RX MEDLINE=92111383; PubMed=1764995;
RA Weinmaster G., Roberts V.J., Lemke G.;
RT "A homolog of Drosophila Notch expressed during mammalian
RT development.";
RL Development 113:199-205(1991).
RN (2)
RN REVISIONS TO 1652-1653.
RA Weinmaster G.;
RL Submitted (APR-1998) to the EMBL/GenBank/DBJ databases.
RN (3)
RP FUNCTION.
RX MEDLINE=21094508; PubMed=11182080;
RA Tanigaki K., Nogaki F., Takahashi J., Tashiro K., Kurooka H.,
RA Honjo T.;
RT "Notch1 and Notch3 instructively restrict bFGF-responsive multipotent
RT neural progenitor cells to an astroglial fate.";
RL Neuron 29:45-55(2001).
RN (4)
RP TISSUE SPECIFICITY.
RX MEDLINE=93202015; PubMed=1295745;
RA Weinmaster G., Roberts V.J., Lemke G.;
RT "Notch2: a second mammalian Notch gene.";
RL Development 116:931-941(1992).
RN (5)
RP TISSUE SPECIFICITY.

```

```

RX MEDLINE=21331789; PubMed=11438922;
RA Irvin D.K., Zurcher S.D., Nguyen T., Weinmaster G., Kornblum H.I.;
RT "Expression patterns of Notch1, Notch2, and Notch3 suggest multiple
RT functional roles for the Notch-Delta signaling system during brain
RT development.";
RL J. Comp. Neurol. 436:167-181(2001).
CC
CC -1- FUNCTION: Functions as a receptor for membrane-bound ligands
CC jagged1, jagged2 and Delta1 to regulate cell-fate determination.
CC Upon ligand activation through the released notch intracellular
CC domain (NICD) it forms a transcriptional activator complex with
CC RBP-J kappa and activates genes of the enhancer of split locus.
CC Affects the implementation of differentiation, proliferation and
CC apoptotic programs (By similarity). Acts instructively to control
CC the cell fate determination of CNS multipotent progenitor cells,
CC resulting in astroglial induction and neuron/oligodendrocyte
CC suppression.
CC -1- SUBUNIT: Heterodimer of a C-terminal fragment N(TM) and a N-
CC terminal fragment N(EC) which are probably linked by disulfide
CC bonds (By similarity).
CC -1- SUBCELLULAR LOCATION: Type I membrane protein. Following
CC proteolytical processing NICD is translocated to the nucleus (By
CC similarity).
CC -1- TISSUE SPECIFICITY: Expressed in the brain, kidney and spleen.
CC Expressed in postnatal central nervous system (CNS) germinal zones
CC and, in early postnatal life, within numerous cells throughout the
CC CNS. Found in both subventricular and ventricular germinal zones.
CC -1- DEVELOPMENTAL STAGE: In the embryo, highest levels occur between
CC days 12 and 14 and decrease rapidly to much lower levels in the
CC adult.
CC -1- PTM: Synthesized in the endoplasmic reticulum as an inactive form
CC which is proteolytically cleaved by a furin-like convertase in the
CC trans-golgi network before it reaches the plasma membrane to yield
CC an active, ligand-accessible form. Cleavage results in a C-
CC terminal fragment N(TM) and a N-terminal fragment N(EC). Following
CC ligand binding, it is cleaved by TNF-alpha converting enzyme
CC (TACE) to yield a membrane-associated intermediate fragment called
CC notch extracellular truncation (NEXT). This fragment is then
CC cleaved by presenilin dependent gamma-secretase to release a
CC notch-derived peptide containing the intracellular domain (NICD)
CC from the membrane (By similarity).
CC -1- PTM: Phosphorylated (By similarity).
CC -1- SIMILARITY: BELONGS TO THE NOTCH FAMILY.
CC -1- SIMILARITY: CONTAINS 36 EGF-LIKE DOMAINS.
CC -1- SIMILARITY: CONTAINS 3 LIN/NOTCH REPEATS.
CC -1- SIMILARITY: CONTAINS 5 ANK REPEATS.
CC
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CC -----
CC DR EMBL: X57405; CAA40667.1; -.
CC DR HSSP: P00740; IEDM.
CC DR InterPro: IPR002110; ANK.
CC DR InterPro: IPR000152; Asx_hydroxyl.
CC DR InterPro: IPR000561; EGF-like.
CC DR InterPro: IPR000742; EGF-2.
CC DR InterPro: IPR001881; EGF-Ca.
CC DR InterPro: IPR001438; EGF-II.
CC DR InterPro: IPR002049; Laminin_EGF.
CC DR InterPro: IPR000800; Notch.
CC DR Pfam: PR00008; EGF_36.
CC DR Pfam: PR00023; ank_6.
CC DR Pfam: PR00066; notch_3.
CC DR PRINTS: PR00010; EGFBLD.
CC DR PRINTS: PR00011; EGFFLAMININ.
CC DR PRINTS: PR01452; NOTCH.
CC DR SMART: SM00248; ANK_5.
CC DR SMART: SM00179; EGF_CA_25.
CC DR SMART: SM00001; EGF_Like; 10.

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Query Match      36.4%; Score 51; DB 1; Length 2531;
Best Local Similarity 36.4%; Pred. No. 13;
Matches 8; Conservative 3; Mismatches 11; Indels 0; Gaps 0;

QY      6 QKCPQHLDDCGCSXXCNXXNKCVCV 27
Db      252 QNCEENVDDCPGNCKNGKAGACV 273

Search completed: January 14, 2003, 18:28:28
Job time : 12 secs

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Search completed: January 14, 2003, 18:28:28  
Job time : 12 secs

Query Match	Score 51;	DB 1;	Length 2531;
Best local similarity	36.4%;		
Matches	8;	Conservative	3;
		Mismatches	11;
		Indels	0;
		Gaps	0;



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OM protein - protein search, using sw model

Run on: January 14, 2003, 18:26:16 ; Search time 29 Seconds

(without alignments)  
191.837 Million cell updates/sec

Title: US-09-666-837B-1-COPY

Perfect score: 140

Sequence: 1 CRIYNQKcFQhLDCCSXKXKXKXCV 27

Scoring table: BLOSUM62

Searched: 671580 seqs, 206047115 residues

Total number of hits satisfying chosen parameters: 671580

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 08

Maximum Match 1008

Listing first 45 summaries

Database :  
1: SP-archaea:\*  
2: SP-bacteria:\*  
3: SP-fungi:\*  
4: SP-human:\*  
5: SP-invertebrate:\*  
6: SP-mammal:\*  
7: SP-mhc:\*  
8: SP-organelle:\*  
9: SP-phage:\*  
10: SP-plant:\*  
11: SP-rodent:\*  
12: SP-virus:\*  
13: SP-vertebrate:\*  
14: SP-unclassified:\*  
15: SP-virus:\*  
16: SP-bacteriap:\*  
17: SP-archaeap:\*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

## SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	56	40.0	752	13	042374 brachydanio
2	55	39.3	664	13	091at6 brachydanio
3	53	37.9	1685	5	0904A2 Q9u4a2 plasmodium
4	52	37.1	642	13	P79941 P79941 xenopus lae
5	52	37.1	2447	13	013149 Iugu rubrip
6	51	36.4	1214	13	090YD2 xenopus lae
7	50	35.7	244	5	09VSG1 Q9vsg1 caenorhabdi
8	50	35.7	354	5	09XV21 Q9xv21 caenorhabdi
9	50	35.7	2653	10	025253 Lucilia cup
10	49	35.0	358	10	091P17 Q91p17 arabidopsis
11	49	35.0	721	13	091902 Q91902 xenopus lae
12	49	35.0	1440	5	020204 caenorhabdi
13	49	35.0	2352	5	061240 halocynthia
14	49	35.0	3623	11	070244 rattus norv
15	48.5	34.6	1208	5	023456 caenorhabdi
16	48	34.3	448	5	Q26107 plasmodium

17	48	34.3	552	5	045117 chironomus
18	48	34.3	1075	5	09NC90 Q9nc90 strongyloce
19	48	34.3	1372	5	P91526 P91526 caenorhabdi
20	48	34.3	2146	5	09VC97 Q9vc97 drosophila
21	48	34.3	2531	5	016004 016004 lytechinus
22	47.5	33.9	53	12	089743 089743 buzura supp
23	47.5	33.9	53	12	09YMH9 Q9ymh9 lymantiria d
24	47	33.6	346	2	08VUT4 Q8vut4 pseudomonas
25	47	33.6	464	5	095RM9 Q95rm9 drosophila
26	47	33.6	530	5	024526 024526 drosophila
27	47	33.6	615	13	057409 057409 brachydanio
28	47	33.6	723	4	090UV2 Q90uv2 homo sapien
29	47	33.6	723	4	09N041 Q9n041 homo sapien
30	47	33.6	1216	13	090Y55 Q90y55 brachydanio
31	47	33.6	1254	13	09YHU2 Q9yhu2 drosophila
32	47	33.6	1254	13	090Y56 Q90y56 brachydanio
33	47	33.6	1290	13	09M6E1 Q9m6e1 gallus gall
34	47	33.6	1316	4	086UT7 Q86ut7 homo sapien
35	47	33.6	1480	5	09VTF8 Q9vtf8 drosophila
36	47	33.6	1504	5	09XVY4 Q9xvy4 drosophila
37	47	33.6	1504	5	09V7P9 Q9v7p9 drosophila
38	47	33.6	1551	5	09NGV4 Q9ngv4 drosophila
39	47	33.6	3396	5	09VM55 Q9vm55 drosophila
40	46.5	33.2	69	5	09UA92 Q9ua92 conus abbre
41	46.5	33.2	69	5	09TVK4 Q9tvk4 conus abbre
42	46.5	33.2	69	5	09TVK3 Q9tvk3 conus abbre
43	46	32.9	778	13	09IBG4 Q9ibg4 xenopus lae
44	46	32.9	1687	11	061204 061204 mus musculu
45	46	32.9	2524	5	Q9GPA5 Q9gpa5 branchiosto

## ALIGNMENTS

RESULT 1  
ID 042374 PRELIMINARY; PRT; 752 AA.  
AC 042374;  
DT 01-JAN-1998 (TREMBLrel. 05, Created)  
DT 01-JAN-1998 (TREMBLrel. 05, Last sequence update)  
DT 01-MAR-2002 (TREMBLrel. 20, Last annotation update)  
DE Notch receptor protein (Fragment).  
GN NOTCH2 OR NOTCH6.  
OS Brachydanio rerio (Zebrafish) (Zebra danio).  
OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
OC Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;  
OC Cyprinidae; Danio.  
OX NCBI\_TaxID=7955;  
RN [1]  
RP SEQUENCE FROM N.A.  
RA Westlin J., Lardelli M.;  
RT "Three novel Notch genes in zebrafish: implications for vertebrate  
RT Notch gene evolution and function.";  
RL Dev. Genes Evol. 207:51-63(1997).  
DR EMBL; Y10354; CAA71380.1; -;  
DR HSSP; P00740; IEDM.  
DR ZFIN; ZDB-GENE-000329-4; notch2.  
DR InterPro; IPR000152; ASX\_hydroxyl.  
DR InterPro; IPR000561; EGF-like.  
DR InterPro; IPR000742; EGF\_2.  
DR InterPro; IPR001881; EGF\_Ca.  
DR InterPro; IPR001438; EGF\_IT.  
DR InterPro; IPR000083; Fibronctn.  
DR InterPro; IPR002049; Laminln\_EGF.  
DR InterPro; IPR000800; Notch.  
DR Pfam; PF00008; EGF; 16.  
DR Pfam; PF00066; notch; 2.  
DR PRINTS; PR00010; EGFBL00D.  
DR PRINTS; PR00011; EGF\_LAMININ.  
DR PRINTS; PR00012; FNTYPEP.  
DR SMART; SM00179; EGF\_Ca; 9.  
DR SMART; SM00001; EGF\_Like; 5.  
DR SMART; SM00004; NL; 2.





RA Beeson K.Y., Benos P.V., Berman B.P., Bhandari D., Bolshakov S.,  
RA Borikova D., Botchan M.R., Bouck J., Brokstein P., Brotter P.,  
RA Butts K.C., Busam D.A., Butler H., Cadieu E., Center A., Chandra I.,  
RA Cherry J.M., Cawley S., Dahle C., Davenport L.B., Davies P.,  
RA de Pablo B., Delcher A., Deng Z., Mays A.D., Dew I., Dietz S.M.,  
RA Dodson K., Doup L.E., Downes M., Dugan-Rocha S., Dunkov B.C., Dunn P.,  
RA Durbin K.J., Evangelista C.C., Ferraz C., Ferreira S., Fleischmann W.,  
RA Foster C., Gabriellian A.E., Garg N.S., Gelbart W.M., Glasser K.,  
RA Glodet A., Gong F., Gorrell J.H., Gu Z., Guan P., Harris M.,  
RA Harris N.L., Harvey D., Helman T.J., Hernandez J.R., Houck J.,  
RA Hostin D., Houston K.A., Howland T.J., Wei M.-H., Idegyan C.,  
RA Jatalil M., Kailush F., Karpen G.H., Ke Z., Kennison J.A., Ketchum K.A.,  
RA Kimmel B.E., Kodira C.D., Kraft C., Kravitz S., Kulp D., Lai Z.,  
RA Lasko P., Lei Y., Levitsky A.A., Li J., Li Z., Liang Y., Lin X.,  
RA Liu X., Mattei B., McIntosh T.C., McLeod M.P., McPherson D.,  
RA Merkulov G., Mlshina N.V., Moharriy C., Morris J., Moshnefti A.,  
RA Mount S.M., Moy M., Murphy B., Murphy L., Muzny D.M., Nelson D.L.,  
RA Nelson D.R., Nelson K.A., Nixon K., Nusskern D.R., Pacleb J.M.,  
RA Palazzolo M., Pittman G.S., Pan S., Pollard J., Purl V., Reese M.G.,  
RA Relenert K., Remington K., Saunders R.D.C., Scheeler F., Shen H.,  
RA Shue B.C., Siden-Klamos I., Simpson M., Skupski M.P., Smith T.,  
RA Spier E., Spradling A.C., Stapleton M., Strong R., Sun E.,  
RA Styrskas R., Tector C., Turner R., Venter E., Wang A.H., Wang X.,  
RA Wang Z.-Y., Wasserman D.A., Weinstock G.M., Weissbach J.,  
RA Williams S.M., Woodage T., Worley K.C., Wu D., Yang S., Yao Q.A.,  
RA Ye J., Yeh R.-F., Zaveri J.S., Zhan M., Zhang G., Zhao Q., Zheng L.,  
RA Zheng X.H., Zhong F.N., Zhong W., Zhou X., Zhu S., Zhu X., Smith H.O.,  
RA Gibbs R.A., Myers E.W., Rubin G.M., Venter J.C.;  
RT "mpe genome sequence of Drosophila melanogaster.";  
RL Science 287:2185-2195(2000).  
DR EMBL: AE003556; AAF50460.2; -.  
DR HSSP: P07260; IAP8.  
DR Playbase: FBgn0035860; CG8023.  
DR InterPro: IPR001040; TIF\_EIF\_4E.  
DR Pfam: PF01652; IFAE; 1.  
DR PROSITE: PS003697; TIF\_EIF\_4E; 1.  
DR PROSITE: PS00813; IFAE; 1.  
SQ SEQUENCE 244 AA; 28492 MW; 2993FE5D94F5AB40 CRC64;

Query Match 35.7%; Score 50; DB 5; Length 244;

Best Local Similarity 44.4%; Pred. No. 1.4;

Matches 8; Conservative 2; Mismatches 8; Indels 0; Gaps 0;

Qy 7 KCFQHLDDCCSXCNXXN 24

Db 169 ECFQSHDEICGVINVRN 186

#### RESULT 8

Q9XV21 PRELIMINARY; PRT; 354 AA.

ID Q9XV21  
AC Q9XV21;  
DT 01-NOV-1999 (TREMblrel. 12, Created)  
DT 01-NOV-1999 (TREMblrel. 12, Last sequence update)  
DT 01-DEC-2001 (TREMblrel. 19, Last annotation update)  
DE F46B3.9 protein.  
GN F46B3.9.  
OS Caenorhabditis elegans.  
OC Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabdilitida; Rhabditiocida;  
OC Rhabdilitida; Pelodierinae; Caenorhabditis.  
OC NCB1\_TaxID=6239;  
RN [1]  
RN [1] SEQUENCE FROM N.A.  
RA Ainscough R.;  
RL Submitted (NOV-1996) to the EMBL/GenBank/DBJ databases.  
RN [2]  
RN [2] SEQUENCE FROM N.A.  
RX MEDLINE=99069613; PubMed=9851916;  
RT none;  
RT "Genome sequence of the nematode C.elegans: A platform for  
RL Science 282:2012-2018(1998).  
DR EMBL: ZB1540; CAB04398.1; -.

DR InterPro: IPR000561; EGF-like.  
DR InterPro: IPR003645; FOIN.  
DR SMART: SM00001; EGF\_1like; 1.  
DR SMART: SM00274; FOLN; 6.  
SQ SEQUENCE 354 AA; 37229 MW; 5769BF095F8E03F9 CRC64;

Query Match 35.7%; Score 50; DB 5; Length 354;

Best Local Similarity 32.1%; Pred. No. 2;

Matches 9; Conservative 4; Mismatches 13; Indels 2; Gaps 1;

Qy 1 CRXN--QKCFQHLDDCCSXCNXXNC 26

Db 158 CKLVNCSKPCVPELDQCSHKISGSHC 185

#### RESULT 9

Q25253 PRELIMINARY; PRT; 2653 AA.

ID Q25253  
AC Q25253;  
DT 01-NOV-1996 (TREMblrel. 01, Created)  
DT 01-NOV-1996 (TREMblrel. 01, Last sequence update)  
DT 01-DEC-2001 (TREMblrel. 19, Last annotation update)  
DE Notch homolog scalloped wings (SCL).  
GN SCL.  
OS Lucilia cuprina (Greenbottle fly) (Australian sheep blowfly).  
OC Eukaryota; Metazoa; Arthropoda; Tracheata; Hexapoda; Insecta;  
OC Eukaryota; Neoptera; Endopterygota; Diptera; Brachycera; Muscomorpha;  
OC Oestrioidea; Calliphoridae; Lucilia.  
RN [1]  
RN [1] SEQUENCE FROM N.A.  
RP STRAIN=SS SEEKING;  
RC MEDLINE=96400928; PubMed=8807304;  
RX Davies A.G., Game A.Y., Chen Z., Williams T.J., Goodall S., Yen J.L.,  
RA McKenzie J.A., Batterham P.;  
RT "scalloped wings is the Lucilia cuprina Notch homologue and a  
RT candidate for the modifier of fitness and asymmetry of diaznon  
RT resistance.";  
RL Genetics 143:1321-1337(1996).  
RN [2]  
RN [2] SEQUENCE OF 39-265 FROM N.A.  
RP STRAIN=SS SEEKING;  
RC Chen Z., McKenzie J.A., Batterham P.;  
RL Submitted (DEC-1997) to the EMBL/GenBank/DBJ databases.  
RN [3]  
RN [3] SEQUENCE OF 39-265 FROM N.A.  
RP STRAIN=SS SEEKING;  
RC Chen Z., McKenzie J.A., Batterham P.;  
RL Submitted (NOV-1997) to the EMBL/GenBank/DBJ databases.  
DR EMBL: U58977; AAC36151.1; -.  
DR EMBL: AF032672; AAC36152.1; -.  
DR EMBL: AF032670; AAC36152.1; JOINED.  
DR EMBL: AF032671; AAC36152.1; JOINED.  
DR EMBL: AF032673; AAC36153.1; -.  
DR HSSP: P00740; IEDM.  
DR InterPro: IPR002110; ANK.  
DR InterPro: IPR000152; Asx\_hydroxyl.  
DR InterPro: IPR000561; EGF-like.  
DR InterPro: IPR000742; EGF-2.  
DR InterPro: IPR001881; EGF-Ca.  
DR InterPro: IPR001438; EGF-II.  
DR InterPro: IPR000800; Notch.  
DR Pfam: PF00023; ank; 6.  
DR Pfam: PF00008; EGF; 36.  
DR Pfam: PF00066; notch; 3.  
DR PRINTS: PR00010; EGFBLDOD.  
DR PRINTS: PR01452; NOTCH.  
DR SMART: SM00248; ANK; 4.  
DR SMART: SM00179; EGF\_CA; 24.  
DR SMART: SM00001; EGF\_1like; 11.  
DR SMART: SM00004; NU; 2.  
DR PROSITE: PS50088; ANK\_REPEAT; 5.  
DR PROSITE: PS50297; ANK\_REPEAT\_REGION; 1.



DR PROSITE; PS00010; ASX\_HYDROXYL; 22.  
 DR PROSITE; PS00022; EGF\_1; UNKNOWN\_34.  
 DR PROSITE; PS01186; EGF\_2; 28.  
 DR PROSITE; PS01187; EGF\_CA; 21.  
 KW ANK repeat; Calcium-binding; EGF-like domain; Glycoprotein;  
 KW Hydroxylation; Repeat  
 SO SEQUENCE 2653 AA; 285928 MW; 6AF2A058FE6C329 CRC64;  
 Query Match  
 Best Local Similarity 31.8%; Score 50; DB 5; Length 2653;  
 Matches 7; Conservative 4; Mismatches 11; Indels 0; Gaps 0;  
 Oy 6 QKCFQHLDDCCSXCNXNXC 27  
 Db 270 KNCBQNIIDCGHLCONGGTCT 291  
 RESULT 10  
 Q9LPI7  
 ID Q9LPI7 PRELIMINARY; PRT; 358 AA.  
 AC Q9LPI7;  
 DT 01-OCT-2000 (TREMBLrel. 15, Created)  
 DT 01-OCT-2000 (TREMBLrel. 15, Last sequence update)  
 DT 01-DEC-2001 (TREMBLrel. 19, Last annotation update)  
 DE FN18.15.  
 OS Arabidopsis thaliana (Mouse-ear cress).  
 OC Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta;  
 OC Spermatophyta; Magnoliophyta; eudicotyledons; core eudicots; Rosidae;  
 OC eurosids II; Brassicales; Brassicaceae; Arabidopsis.  
 OC NCBI\_Taxid=3702;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Chao Q., Brooks S., Buehler E., Johnson-Hopson C., Khan S., Kim C.,  
 RA Shih P., Altairi H., Bei Q., Chin C., Chlou J., Choi E., Conn L.,  
 RA Conway A., Gonzales A., Hansen N., Howing B., Koo T., Lam B., Lee J.,  
 RA Lanz C., Li J., Liu K., Liu S., Mukharsky N., Nguyen M.,  
 RA Palm C., Pham P., Sakano H., Schwartz J., Southwick A., Thaveri A.,  
 RA Toriumi M., Vaysberg M., Yu G., Federspiel N.A., Theologis A.,  
 RA Ecker J.R.;  
 RT "Genomic sequence for Arabidopsis thaliana BAC FN18 from chromosome  
 I.";  
 RL Submitted (JAN-2001) to the EMBL/GenBank/DBJ databases.  
 DR EMBL; AC017118; AAP25976.1;  
 DR InterPro; IPR003441; NAM.  
 DR Pfam; PF02365; NAM; 1.  
 SO SEQUENCE 358 AA; 41520 MW; 3C6F27668B0140F5 CRC64;  
 Query Match  
 Best Local Similarity 46.7%; Score 49; DB 10; Length 358;  
 Matches 7; Conservative 4; Mismatches 4; Indels 0; Gaps 0;  
 Oy 1 CRXNCRFQHLDDC 15  
 Db 172 CRVFRKKNYOKIDDC 186  
 RESULT 11  
 Q91902  
 ID Q91902 PRELIMINARY; PRT; 721 AA.  
 AC Q91902;  
 DT 01-NOV-1996 (TREMBLrel. 01, Created)  
 DT 01-NOV-1996 (TREMBLrel. 01, Last sequence update)  
 DT 01-DEC-2001 (TREMBLrel. 19, Last annotation update)  
 DE X-delta-1.  
 OS Xenopus laevis (African clawed frog).  
 OC Eukaryota; Metazoa; Chordata; Vertebrata; Euteleostomi;  
 OC Amphibia; Batrachia; Anura; Mesobatrachia; Pipiloidea; Pipidae;  
 OC Xenopodidae; Xenopus.  
 OC NCBI\_Taxid=8355;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=95319507; PubMed=7596411;  
 RA Henrique D., Adam J., Myat A., Chltnis A., Lewis J., Ish-Horowitz D.;

RT "Expression of a Delta homologue in prospective neurons in the  
 RT chick.";  
 RL Nature 375:787-790(1995).  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=95319503; PubMed=7596407;  
 RA Chltnis A., Henrique D., Lewis J., Ish-Horowitz D., Kintner C.;  
 RT "Primary neurogenesis in Xenopus embryos regulated by a homologue of  
 RT the Drosophila neurogenic gene Delta.";  
 RL Nature 375:761-766(1995).  
 SO EMBL; L42229; AAC38017.1;  
 DR HSSP; P00740; 1EDM.  
 DR InterPro; IPR000152; Asx\_hydroxyl.  
 DR InterPro; IPR001774; DSL.  
 DR InterPro; IPR000561; EGF\_1like.  
 DR InterPro; IPR000742; EGF\_2.  
 DR InterPro; IPR001881; EGF\_CA.  
 DR InterPro; IPR001438; EGF\_11.  
 DR Pfam; PF01414; DSL; 1.  
 DR Pfam; PF00008; EGF; 8.  
 DR PRINTS; PR00010; EGFBL00D.  
 DR SMART; SM00051; DSL; 1.  
 DR SMART; SM00179; EGF\_CA; 4.  
 DR SMART; SM00001; EGF\_1like; 4.  
 DR PROSITE; PS00001; ASX\_HYDROXYL; UNKNOWN\_3.  
 DR PROSITE; PS00022; EGF\_1; UNKNOWN\_8.  
 DR PROSITE; PS01187; EGF\_CA; 2.  
 KW Calcium-binding; EGF-like domain; Glycoprotein; Repeat.  
 SO SEQUENCE 721 AA; 79922 MW; 9EBDC85C439DD194 CRC64;  
 Query Match  
 Best Local Similarity 38.1%; Score 49; DB 13; Length 721;  
 Matches 8; Conservative 2; Mismatches 11; Indels 0; Gaps 0;  
 Oy 6 QKCFQHLDDCCSXCNXNXC 26  
 Db 440 RNCDDNIDDCSTFPCONGSTC 460  
 RESULT 12  
 Q20204  
 ID Q20204 PRELIMINARY; PRT; 1440 AA.  
 AC Q20204;  
 DT 01-NOV-1996 (TREMBLrel. 01, Created)  
 DT 01-MAY-2000 (TREMBLrel. 13, Last sequence update)  
 DT 01-JUN-2002 (TREMBLrel. 21, Last annotation update)  
 DE F40E10.4 protein.  
 GN F40E10.4.  
 OS Caenorhabditis elegans.  
 OC Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditoidea;  
 OC Rhabditidae; Peloderinae; Caenorhabditis.  
 OC NCBI\_Taxid=6239;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA Smye R.;  
 RL Submitted (FEB-1996) to the EMBL/GenBank/DBJ databases.  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=99069613; PubMed=9851916;  
 RA none;  
 RT "Genome sequence of the nematode C. elegans: A platform for  
 RT investigating biology.";  
 RL Science 282:2012-2018(1998).  
 RN [3]  
 RP SEQUENCE FROM N.A.  
 RA Smye R.;  
 RL Submitted (MAR-1998) to the EMBL/GenBank/DBJ databases.  
 DR EMBL; Z69792; CAA93668.2;  
 DR EMBL; AL022270; CAA93668.2; JOINED.  
 DR EMBL; AL022270; CAB63434.1;  
 DR EMBL; Z69792; CAB63434.1; JOINED.  
 DR HSSP; P00740; 1EDM.

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DR InterPro: IPR000152; Asx_hydroxyl.
DR InterPro: IPR000359; Cys_knot.
DR InterPro: IPR000561; EGF_1like.
DR InterPro: IPR000742; EGF_2.
DR InterPro: IPR001881; EGF_Ca.
DR InterPro: IPR001438; EGF_II.
DR InterPro: IPR001791; Laminin_G.
DR InterPro: IPR001611; LRR.
DR InterPro: IPR000483; LRR_Cterm.
DR InterPro: IPR000372; LRR_Nterm.
DR InterPro: IPR003592; LRR_out.
DR InterPro: IPR003591; LRR_tyr.
DR Pfam: PF00008; EGF_7.
DR Pfam: PF00054; Laminin_G; 1.
DR Pfam: PF00560; LRR; 18.
DR Pfam: PF01463; LRRCT; 4.
DR Pfam: PF01462; LRRNT; 4.
DR PRINTS: PR00010; EGFBL00D.
DR PRINTS: PR00019; LEURICHRPT.
DR SMART: SM00041; CT; 1.
DR SMART: SM00179; EGF_CA; 2.
DR SMART: SM00001; EGF_1like; 5.
DR SMART: SM00282; Lang; 1.
DR SMART: SM00370; LRR; 3.
DR SMART: SM00082; LRRCT; 4.
DR SMART: SM00013; LRRNT; 4.
DR SMART: SM00369; LRR_TYP; 7.
DR PROSITE: PS00010; ASX_HYDROXYL; UNKNOWN_1.
DR PROSITE: PS01225; CTCK_2; 1.
DR PROSITE: PS00022; EGF_1; UNKNOWN_7.
DR PROSITE: PS01186; EGF_2; 5.
DR PROSITE: PS01187; EGF_CA; 1.
DR Calcium-binding; EGF-like domain; Glycoprotein; Repeat.
KW SEQUENCE 1440 AA; 161942 MW; 0B5D198645D3670 CRC64.

Query Match 35.0%; Score 49; DB 5; Length 1440;
Best Local Similarity 35.0%; Pred. No. 10;
Matches 7; Conservative 4; Mismatches 9; Indels 0; Gaps 0;

Qy 8 CF0HLDCCSXXCNXNCV 27
Db 944 CEKNIDCVSKENGKCV 963

RESULT 13
061240 PRELIMINARY; PRT; 2352 AA.
AC 061240.
DT 01-AUG-1998 (TREMBlrel. 07, Created)
DT 01-AUG-1998 (TREMBlrel. 07, Last sequence update)
DT 01-DEC-2001 (TREMBlrel. 19, Last annotation update)
DE Hrnotch protein.
GN HRNOTCH.
OS Halocynthia roretzi (Sea squirt).
OC Eukaryota; Metazoa; Chordata; Urochordata; Ascidiacea;
OC Stolidobranchia; Pyuridae; Halocynthia.
OX NCBI_TaxID=7729;
RX [1]
RP SEQUENCE FROM N.A.
RA Hori S., Satoh T., Matsumoto M., Makabe K.W., Nishida H.;
RT "Notch homologue from Halocynthia roretzi is preferentially expressed
RL in the central nervous system during ascidian embryogenesis."
DR HMBL: AB001327; BAA2571.1; -.
DR HMBL: P00740; IEDM.
DR InterPro: IPR002110; ANK.
DR InterPro: IPR000152; Asx_hydroxyl.
DR InterPro: IPR000561; EGF_1like.
DR InterPro: IPR000742; EGF_2.
DR InterPro: IPR001881; EGF_Ca.
DR InterPro: IPR001438; EGF_II.
DR InterPro: IPR000800; Notch.
DR Pfam: PF00023; ank; 6.

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DR Pfam: PF00008; EGF; 32.
DR Pfam: PF00066; notch; 3.
DR PRINTS: PR00010; EGFBL00D.
DR PRINTS: PR01452; NOTCH.
DR SMART: SM00248; ANK; 5.
DR SMART: SM00179; EGF_CA; 17.
DR SMART: SM00001; EGF_1like; 9.
DR SMART: SM00004; NL; 2.
DR PROSITE: PS50088; ANK_REPEAT; 5.
DR PROSITE: PS50297; ANK_REPEAT_REGION; 1.
DR PROSITE: PS00010; ASX_HYDROXYL; 18.
DR PROSITE: PS00022; EGF_1; UNKNOWN_28.
DR PROSITE: PS01186; EGF_2; 22.
DR PROSITE: PS01187; EGF_CA; 18.
KW ANK repeat; Calcium-binding; EGF-like domain; Glycoprotein;
KW Hydroxylation; Repeat.
KW SEQUENCE 2352 AA; 252623 MW; 13D1C056B0D08D CRC64;

Query Match 35.0%; Score 49; DB 5; Length 2352;
Best Local Similarity 35.0%; Pred. No. 16;
Matches 7; Conservative 4; Mismatches 9; Indels 0; Gaps 0;

Qy 8 CF0HLDCCSXXCNXNCV 27
Db 452 CSONIDECASIPCMKATCI 471

RESULT 14
070244 PRELIMINARY; PRT; 3623 AA.
AC 070244.
DT 01-AUG-1998 (TREMBlrel. 07, Created)
DT 01-JAN-1999 (TREMBlrel. 09, Last sequence update)
DT 01-JUN-2002 (TREMBlrel. 21, Last annotation update)
DE Intrinsic factor-B12 receptor precursor.
GN CUBILIN.
OS Rattus norvegicus (Rat).
OC Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX NCBI_TaxID=10116;
RX [1]
RP SEQUENCE FROM N.A.
RA MEDLINE=98148073; PubMed=9478979;
RA Moestrup S.K., Koziyaki R., Kristiansen M., Kaysen J.H.,
RA Rasmussen H.H., Brault D., Pontillon F., Goda F.O., Christensen E.I.,
RA Hammond T.G., Verroust P.J.;
RT "The intrinsic factor-vitamin B12 receptor and target of teratogenic
RT antibodies is a megalin-binding peripheral membrane protein with
RT homology to developmental proteins."
RL J. Biol. Chem. 273:5235-5242(1998).
CC -1- SIMILARITY: CONTAINS 26 CUB DOMAINS.
DR HMBL: AF022247; MAC71661.1; -.
DR HMBL: P00740; IEDM.
DR InterPro: IPR000152; Asx_hydroxyl.
DR InterPro: IPR000859; CUB_domain.
DR InterPro: IPR000561; EGF_1like.
DR InterPro: IPR000742; EGF_2.
DR InterPro: IPR001881; EGF_CA.
DR Pfam: PF00431; CUB; 27.
DR Pfam: PF00008; EGF; 7.
DR SMART: SM00042; CUB; 26.
DR SMART: SM00179; EGF_CA; 4.
DR SMART: SM00001; EGF_1like; 4.
DR PROSITE: PS00010; ASX_HYDROXYL; 3.
DR PROSITE: PS01180; CUB; 27.
DR PROSITE: PS00022; EGF_1; UNKNOWN_4.
DR PROSITE: PS01186; EGF_2; 2.
DR PROSITE: PS01187; EGF_CA; 4.
KW Calcium-binding; EGF-like domain; Glycoprotein; Hydroxylation;
KW Receptor; Repeat; signal.
FT SIGNAL 1
FT CHAIN 21 3623
FT SEQUENCE 3623 AA; 398981 MW; 39FB92AC6545240 CRC64;

```

Query Match 35.08; Score 49; DB 11; Length 3623;  
 Best Local Similarity 31.8%; Pred. No. 23;  
 Matches 7; Conservative 5; Mismatches 10; Indels 0; Gaps 0;

OY 6 OKCFQHLDDCGSXKXNXXNCV 27  
 DB 427 ONCTENINDCSSNPCLNGCTCI 448

## RESULT 15

O23456 PRELIMINARY; PRT; 1208 AA.  
 AC O23456:  
 DT 01-NOV-1996 (TRENBLREL. 01, Created)  
 DT 01-NOV-1996 (TRENBLREL. 01, Last sequence update)  
 DT 01-JUN-2002 (TRENBLREL. 21, Last annotation update)  
 DE ZK287.4 protein.  
 GN ZK287.4.  
 OS Caenorhabditis elegans.  
 OC Eukaryota; Metazoa; Nematoda; Chromadorea; Rhabditida; Rhabditioidea;  
 OC Rhabditidae; Peloderinae; Caenorhabditis.  
 OX NCBI\_TaxID=6239;  
 RN [1]  
 RP SEQUENCE FROM N.A.  
 RA McMurray A.A.;  
 RL Submitted (APR-1996) to the EMBL/GenBank/DBJ databases.  
 RN [2]  
 RP SEQUENCE FROM N.A.  
 RX MEDLINE=99069613; PubMed=9851916;  
 RA none;  
 RT "Genome sequence of the nematode C.elegans: A platform for  
 RT investigating biology.";  
 RT Science 282:2012-2018(1998).  
 DR EMBL: Z70757; CA94800.1; -.  
 DR HSSP; P31713; ISHP.  
 DR InterPro; IPR002223; Kunitz\_BPTI.  
 DR InterPro; IPR002899; WRI/EB.  
 DR Pfam; PF00014; Kunitz\_BPTI; 7.  
 DR PRINTS; PR00759; BASICPTASE.  
 DR ProDom; PD000222; Kunitz\_BPTI; 6.  
 DR SMART; SM00131; KU; 7.  
 DR SMART; SM00289; WRI; 3.  
 DR PROSITE; PS50279; BPTI\_KUNITZ\_2; 7.  
 DR Serine protease inhibitor.  
 KW SEQUENCE 1208 AA; 133055 MW; F5BABF7D81BDE229 CRC64;

Query Match 34.6%; Score 48.5; DB 5; Length 1208;

Best Local Similarity 45.5%; Pred. No. 10;  
 Matches 10; Conservative 0; Mismatches 11; Indels 1; Gaps 1;

OY 5 NOKCFQHLDDCGSXKXNXXNCV 26  
 DB 805 NONNFQSFDS-CSRACGATNVC 825

Search completed: January 14, 2003, 18:29:05  
 Job time : 32 secs

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## Sequence Family Search of Proteins (/sqsf)

In the sequence family search, each amino acid in the query has to match either the exact amino acid or a family member equivalent, as shown in the Family Equivalence Table below. The Family Equivalence Table is applied only to each common amino acid in the sequence. Specific uncommon amino acids may be included in the sequence; however, family equivalents only exist for the common amino acids. An amino acid family is based on a conservative substitution of amino acids sharing a similar chemical property. Each common amino acid in the query is converted to its family class members in a search. A match occurs on a query sequence if each amino acid is exactly matched or any of its family members are encountered. For example, the Hydrophobic-Aromatic family consists of the common amino acids F, W, and Y. If the amino acid F is specified within a sequence exact family search, it will match on amino acids F, W, or Y.

### FAMILY EQUIVALENCE TABLE

Family Class Name	Family Class Members
Neutral-Weakly Hydrophobic	Ala (A), Gly (G), Pro (P), Ser (S), Thr (T)
Hydrophilic-Acid Amine	Asn (N), Asp (D), Gln (Q), Glu (E)
Hydrophilic-Basic	Arg ( R), His (H), Lys (K)
Hydrophobic	Ile (I), Met (M), Leu (L), Val (V)
Hydrophobic-Aromatic	Phe (F), Trp (W), Tyr (Y)
Crosslinking	Cys ( C)



=> fil reg; d que 12

FILE 'REGISTRY' ENTERED AT 08:39:59 ON 15 JAN 2003  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 14 JAN 2003 HIGHEST RN 479024-64-1  
DICTIONARY FILE UPDATES: 14 JAN 2003 HIGHEST RN 479024-64-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

(L2 12 SEA FILE=REGISTRY ABB=ON CRI'HYP'NQKCFQHLDDCCS/SQSFP )

=> d rn cn sql kwic nte 12 1-12; fil capl; s 12

L2 ANSWER 1 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 332843-22-8) REGISTRY - *Use registry # to match sequence to citation - CA reference #3*

CN Peptide, (Cys-Arg-Ile-Xaa-Asn-Gln-Lys-Cys-Phe-Gln-His-Leu-Asp-Cys-Cys-  
Ser-Xaa-Xaa-Cys-Asn-Xaa-Xaa-Asn-Xaa-Cys-Val) (9CI) (CA INDEX NAME)

*Sequence length*  
SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSXXC NXXNXCXV

=====

HITS-AT: 1-17

NTE

type	location	description
uncommon	Hyp-4	-
uncommon	Aaa-18	-
uncommon	Aaa-19	-
uncommon	Aaa-22	-
uncommon	Aaa-23	-
uncommon	Aaa-25	-

L2 ANSWER 2 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-80-3) REGISTRY - *CA answer #3*

CN L-Alanine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-  
asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminyl-L-  
histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-  
cysteinyl-L-seryl-L-arginyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-  
phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSRKC NRFNKCA

HITS AT: 1-17

NTE

type	location	description
bridge	Cys-1 - Cys-16	disulfide bridge
bridge	Cys-8 - Cys-20	disulfide bridge
bridge	Cys-15 - Cys-26	disulfide bridge
uncommon	Hyp-4 -	-

L2 ANSWER 3 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-76-7 REGISTRY CA reference # 3

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminyl-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-arginyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-phenylalanyl-L-alanyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSRKC NRFAKCV

HITS AT: 1-17

NTE

type	location	description
bridge	Cys-1 - Cys-16	disulfide bridge
bridge	Cys-8 - Cys-20	disulfide bridge
bridge	Cys-15 - Cys-26	disulfide bridge
uncommon	Hyp-4 -	-

L2 ANSWER 4 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-75-6 REGISTRY CA reference # 3

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminyl-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-alanyl-L-arginyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCARKC NRFNKCVC

HITS AT: 1-17

NTE

type	location	description
bridge	Cys-1 - Cys-16	disulfide bridge
bridge	Cys-8 - Cys-20	disulfide bridge
bridge	Cys-15 - Cys-26	disulfide bridge
uncommon	Hyp-4 -	-

L2 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-74-5 REGISTRY CA reference # 3

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-



asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminyl-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-arginyl-L-lysyl-L-cysteinyl-L-alanyl-L-arginyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSRKC ARFNKCV

=====

HITS AT: 1-17

NTE

type	location		description
bridge	Cys-1	- Cys-16	disulfide bridge
bridge	Cys-8	- Cys-20	disulfide bridge
bridge	Cys-15	- Cys-26	disulfide bridge
uncommon	Hyp-4	-	-

L2 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-69-8 REGISTRY *CA reference #3*

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-tyrosyl-L-glutaminyl-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-arginyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCYQ HLDDCCSRKC NRFNKCV

=====

HITS AT: 1-17

NTE

type	location		description
bridge	Cys-1	- Cys-16	disulfide bridge
bridge	Cys-8	- Cys-20	disulfide bridge
bridge	Cys-15	- Cys-26	disulfide bridge
uncommon	Hyp-4	-	-

L2 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-66-5 REGISTRY *CA reference #3*

CN L-Valine, L-cysteinyl-L-lysyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminyl-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-arginyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CKIXNQKCFQ HLDDCCSRKC NRFNKCV

=====

HITS AT: 1-17

NTE

type	location		description
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bridge	Cys-1	- Cys-16	disulfide bridge
bridge	Cys-8	- Cys-20	disulfide bridge
bridge	Cys-15	- Cys-26	disulfide bridge
uncommon	Hyp-4	-	-

L2 ANSWER 8 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-65-4 REGISTRY CA reference # 3

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminyl-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-arginyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-phenylalanyl-L-asparaginyl-L-alanyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSRKC NRFNACV

HITS AT: 1-17

NTE

type	location		description
bridge	Cys-1	- Cys-16	disulfide bridge
bridge	Cys-8	- Cys-20	disulfide bridge
bridge	Cys-15	- Cys-26	disulfide bridge
uncommon	Hyp-4	-	-

L2 ANSWER 9 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-62-1 REGISTRY CA reference # 3

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminyl-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-arginyl-L-alanyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSRAC NRFNKC

HITS AT: 1-17

NTE

type	location		description
bridge	Cys-1	- Cys-16	disulfide bridge
bridge	Cys-8	- Cys-20	disulfide bridge
bridge	Cys-15	- Cys-26	disulfide bridge
uncommon	Hyp-4	-	-

L2 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-60-9 REGISTRY CA reference # 3

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminyl-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminyl-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-arginyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-alanyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA  
INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSRKC NAFNKCVC

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HITS AT: 1-17

NTE

type	location	description
bridge	Cys-1 - Cys-16	disulfide bridge
bridge	Cys-8 - Cys-20	disulfide bridge
bridge	Cys-15 - Cys-26	disulfide bridge
uncommon	Hyp-4 -	-

L2 ANSWER 11 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 331640-59-6 REGISTRY *CA reference # 3*

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminy-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminy-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-alanyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide) (9CI) (CA INDEX NAME)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSAKC NRFNKCVC

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HITS AT: 1-17

NTE

type	location	description
bridge	Cys-1 - Cys-16	disulfide bridge
bridge	Cys-8 - Cys-20	disulfide bridge
bridge	Cys-15 - Cys-26	disulfide bridge
uncommon	Hyp-4 -	-

L2 ANSWER 12 OF 12 REGISTRY COPYRIGHT 2003 ACS

RN 196605-79-57 REGISTRY *CA references 1-11*

CN .kappa.-Conotoxin P VIIA (9CI) (CA INDEX NAME)

OTHER NAMES:

CN L-Valine, L-cysteinyl-L-arginyl-L-isoleucyl-(4R)-4-hydroxy-L-prolyl-L-asparaginyl-L-glutaminy-L-lysyl-L-cysteinyl-L-phenylalanyl-L-glutaminy-L-histidyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-cysteinyl-L-cysteinyl-L-seryl-L-arginyl-L-lysyl-L-cysteinyl-L-asparaginyl-L-arginyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-cysteinyl-, cyclic  
(1.fwdarw.16), (8.fwdarw.20), (15.fwdarw.26)-tris(disulfide)

SQL 27

SEQ 1 CRIXNQKCFQ HLDDCCSRKC NRFNKCVC

=====

HITS AT: 1-17

NTE

type	location	description
bridge	Cys-1 - Cys-16	disulfide bridge
bridge	Cys-8 - Cys-20	disulfide bridge
bridge	Cys-15 - Cys-26	disulfide bridge
uncommon	Hyp-4 -	-

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FILE COVERS 1907 - 15 Jan 2003 VOL 138 ISS 3  
FILE LAST UPDATED: 14 Jan 2003 (20030114/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L3 11 L2 ) *Registry file answer set crossed into CAPLUS to get citations*  
=> d ibib ab hitrn 1-11; fil hom

L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2002:420792 CAPLUS  
DOCUMENT NUMBER: 137:136264  
TITLE: Inhibition of single Shaker K channels by  
.kappa.-conotoxin-PVIIA  
AUTHOR(S): Naranjo, David  
CORPORATE SOURCE: Instituto de Fisiologia Celular, Universidad Nacional  
Autonoma de Mexico, Circuito Exterior, Mexico, 04510,  
Mex.  
SOURCE: Biophysical Journal (2002), 82(6), 3003-3011  
CODEN: BIOJAU; ISSN: 0006-3495  
PUBLISHER: Biophysical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB .kappa.-Conotoxin-PVIIA (.kappa.-PVIIA) is a 27-residue basic (+4) peptide from the venom of the predator snail *Conus purpurascens*. A single .kappa.-PVIIA mol. interrupts ion conduction by binding to the external mouth of Shaker K channels. The blockade of Shaker by .kappa.-PVIIA was studied at the single channel level in membrane patches from *Xenopus* oocytes. The amplitudes of blocked and closed events were undistinguishable, suggesting that the toxin interrupts ion conduction completely. Between -20 and 40 mV .kappa.-PVIIA increased the latency to the first opening by one order of magnitude in a concn.-independent fashion. Because .kappa.-PVIIA has higher affinity for the closed channels at high enough concn. to block >90% of the resting channels, the disocn. rate could be estd. from the anal. of the first latency. At 0 mV, the disocn. rate was 20 s<sup>-1</sup> and had an effective valence of 0.64. The apparent closing rate increased linearly with [.kappa.-PVIIA] indicating an assocn. rate of 56 .mu.M<sup>-1</sup> s<sup>-1</sup>. The toxin did not modify the fraction of null traces. This result suggests that the structural rearrangements in the external mouth contributing to the slow inactivation preserve the main geometrical features of the toxin-receptor interaction.

*Use Registry # to match citation to sequence in Registry record*

IT 196605-79-5, .kappa.-Conotoxin-PVIIA

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibition of single Shaker K channels by .kappa.-conotoxin-PVIIA)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:872474 CAPLUS

DOCUMENT NUMBER: 136:258891

TITLE: Molecular simulation of the interaction of  
.kappa.-conotoxin-PVIIA with the Shaker potassium  
channel pore

AUTHOR(S): Moran, Oscar

CORPORATE SOURCE: CNR, Istituto di Cibernetica e Biofisica, Genoa,  
16149, Italy

SOURCE: European Biophysics Journal (2001), 30(7), 528-536  
CODEN: EBJOE8; ISSN: 0175-7571

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mol. simulation techniques were applied to predict the interaction of the voltage-dependent Shaker potassium channel with the channel-blocking toxin .kappa.-conotoxin-PVIIA (PVIIA). A structural three-dimensional model of the extracellular vestibule of the potassium channel was constructed based on structural homologies with the bacterial potassium channel Kcsa, whose structure has been solved by x-ray crystallog. The docking of the PVIIA mol. was obtained by a geometric recognition algorithm, yielding 100 possible conformations. A series of residue-residue distance restraints, predicted from mutation-cycle expts., were used to select a small set of a plausible channel-toxin complex models among the resulting possible conformations. The four final conformations, with similar characteristics, can explain most of the single-point mutation expts. done with this system. The models of the Shaker-PVIIA interaction predict two clusters of amino acids, crit. for the binding of the toxin to the channel. The first cluster is the amino acids R2, I3, Q6 and K7 that form the plug of the toxin that interacts with the entrance to the selectivity filter of the channel. The second cluster of residues, R22, F23, N24 and K25, interacts with a channel region near to the external entrance of the pore vestibule. The consistency of the obtained models and the exptl. data indicate that the Shaker-PVIIA complex model is reasonable and can be used in further biol. studies such as the rational design of blocking agents of potassium channels and the mutagenesis of both toxins and potassium channels.

IT 196605-79-5, .kappa.-Conotoxin-PVIIA

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study)

(complexes with potassium channel; mol. simulation of the interaction  
of .kappa.-conotoxin-PVIIA with the Shaker potassium channel pore)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:228916 CAPLUS

DOCUMENT NUMBER: 134:275775

TITLE: .kappa.-Conotoxin PVIIA and analogs and derivatives  
for activating ATP-sensitive potassium channels, and  
therapeutic use

INVENTOR(S): Cornell-Bell, Ann H.; Pemberton, Karen E.; Temple,  
Davis L., Jr.; Layer, Richard T.; McCabe, R. Tyler;  
Jones, Robert R.

PATENT ASSIGNEE(S): Cognetix, Inc., USA

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021648	A1	20010329	WO 2000-US25827	20000921
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1218407	A1	20020703	EP 2000-965219	20000921
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRIORITY APPLN. INFO.:			US 1999-155135P	P 19990922
			US 2000-219438P	P 20000720
			WO 2000-US25827	W 20000921
OTHER SOURCE(S): MARPAT 134:275775				
AB	The invention relates to uses of .kappa.-conotoxin PVIIA, analogs and derivs. for activating ATP-sensitive potassium channels. The activation of ATP-sensitive potassium channels is useful for opening KATP channels which can be used to treat a wide range of disease and injury states, including cerebral and cardiac ischemia and asthma.			
IT	331640-59-6 331640-59-6D, derivs. 331640-60-9 331640-60-9D, derivs. 331640-62-1 331640-62-1D , derivs. 331640-65-4 331640-65-4D, derivs. 331640-66-5 331640-66-5D, derivs. 331640-69-8 331640-69-8D, derivs. 331640-74-5 331640-74-5D , derivs. 331640-75-6 331640-75-6D, derivs. 331640-76-7 331640-76-7D, derivs. 331640-80-3 331640-80-3D, derivs. 332843-22-8 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (.kappa.-conotoxin PVIIA and analogs and derivs. for activating ATP-sensitive potassium channels, and therapeutic use)			
IT	196605-79-5, .kappa.-CONOTOXIN P VIIA 196605-79-5D, .kappa.-CONOTOXIN P VIIA, analogs and derivs. RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (.kappa.-conotoxin PVIIA and analogs and derivs. for activating ATP-sensitive potassium channels, and therapeutic use)			
REFERENCE COUNT:	2	THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		
L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS				
ACCESSION NUMBER:	2000:579029 CAPLUS			
DOCUMENT NUMBER:	133:292139			
TITLE:	Single amino acid substitutions in .kappa.-Conotoxin PVIIA disrupt interaction with the Shaker K <sup>+</sup> channel			
AUTHOR(S):	Jacobsen, Richard B.; Koch, E. Dietlind; Lange-Malecki, Bettina; Stocker, Martin; Verhey, Janko; Van Wagoner, Ryan M.; Vyazovkina, Alexandra; Olivera, Baldomero M.; Terlau, Heinrich			
CORPORATE SOURCE:	Departments of Biology and Medicinal Chemistry, University of Utah, Salt Lake City, UT, 84112, USA			

SOURCE: Journal of Biological Chemistry (2000), 275(32),  
24639-24644  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular  
Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB .kappa.-Conotoxin PVIIA (.kappa.-PVIIA), a 27-amino acid peptide with  
three disulfide crosslinks, isolated from the venom of *Conus purpurascens*,  
is the first conopeptide shown to inhibit the Shaker K<sup>+</sup> channel.  
Recently, two groups independently detd. the soln. structure for  
.kappa.-PVIIA using NMR; although the structures reported were similar,  
two mutually exclusive models for the interaction of the peptide with the  
Shaker channel were proposed. The authors carried out a  
structure/function anal. of .kappa.-PVIIA, with alanine substitutions for  
all amino acids postulated to be key residues by both groups. The  
authors' data are consistent with the crit. dyad model developed by Menez  
and co-workers for polypeptide antagonists of K<sup>+</sup> channels. In the case of  
.kappa.-PVIIA, Lys7 and Phe9 are essential for activity as predicted by  
Savarin et al. these workers also correctly predicted an important role  
for Lys25. Thus, although .kappa.-conotoxin PVIIA has no obvious sequence  
homol. to polypeptide toxins from other venomous animals that interact  
with voltage-gated K<sup>+</sup> channels, there may be convergent functional  
features in diverse K<sup>+</sup> channel polypeptide antagonists.  
IT 196605-79-5, .kappa.-Conotoxin P VIIA  
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL  
(Biological study)  
(single amino acid substitutions in .kappa.-Conotoxin PVIIA disrupt  
interaction with the Shaker K<sup>+</sup> channel)  
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2000:191100 CAPLUS  
DOCUMENT NUMBER: 132:237373  
TITLE: Preparation of cyclized conotoxin peptides  
INVENTOR(S): Craik, David James; Daly, Norelle Lee; Nielsen,  
Katherine Justine  
PATENT ASSIGNEE(S): University of Queensland, Australia  
SOURCE: PCT Int. Appl., 43 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015654	A1	20000323	WO 1999-AU769	19990914
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9960705	A1	20000403	AU 1999-60705	19990914
AU 747006	B2	20020509		
EP 1129106	A1	20010905	EP 1999-947111	19990914
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

## PRIORITY APPLN. INFO.:

AU 1998-5895      A 19980914  
WO 1999-AU769      W 19990914

AB Cyclized conotoxin peptides were prep'd. for the therapeutic treatment of mammals. Thus, cyclo[CKGKGAKCSRLMYDCCTGSCRSGKCTRNLPG], a cyclic analog of MVIIA having the linking moiety TRNLPG, was prep'd. by the solid-phase method.

IT 196605-79-5DP, .kappa.-Conotoxin P VIIA, cyclic analogs

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of cyclized conotoxin peptides)

REFERENCE COUNT: 2      THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:477426 CAPLUS

DOCUMENT NUMBER: 131:253554

TITLE: A marine snail neurotoxin shares with scorpion toxins a convergent mechanism of blockade on the pore of voltage-gated K channels

AUTHOR(S): Garcia, Esperanza; Scanlon, Martin; Naranjo, David  
CORPORATE SOURCE: Centro de Investigaciones Biomedicas, Universidad de Colima, Colima, 28045, Mex.

SOURCE: Journal of General Physiology (1999), 114(1), 141-157  
CODEN: JGPLAD; ISSN: 0022-1295

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB .kappa.-Conotoxin-PVIIA (.kappa.-PVIIA) belongs to a family of peptides derived from a hunting marine snail that targets to a wide variety of ion channels and receptors. .kappa.-PVIIA is a small, structurally constrained, 27-residue peptide that inhibits voltage-gated K channels. Three disulfide bonds shape a characteristic four-loop folding. The spatial localization of pos. charged residues in .kappa.-PVIIA exhibits strong structural mimicry to that of charybdotoxin, a scorpion toxin that occludes the pore of K channels. The authors studied the mechanism by which this peptide inhibits Shaker K channels expressed in *Xenopus* oocytes with the N-type inactivation removed. Chronically applied to whole oocytes or outside-out patches, .kappa.-PVIIA inhibition appears as a voltage-dependent relaxation in response to the depolarizing pulse used to activate the channels. At any applied voltage, the relaxation rate depended linearly on the toxin concn., indicating a bimol. stoichiometry. Time consts. and voltage dependence of the current relaxation produced by chronic applications agreed with that of rapid applications to open channels. Effective valence of the voltage dependence,  $z_{\text{delta}}$ , is .apprx.0.55 and resides primarily in the rate of dissocn. from the channel, while the assocn. rate is voltage independent with a magnitude of 107-108 M<sup>-1</sup>s<sup>-1</sup>, consistent with diffusion-limited binding. Compatible with a purely competitive interaction for a site in the external vestibule, tetraethylammonium, a well-known K-pore blocker, reduced .kappa.-PVIIA's assocn. rate only. Removal of internal K<sup>+</sup> reduced, but did not eliminate, the effective valence of the toxin dissocn. rate to a value <0.3. This trans-pore effect suggests that: (a) as in the .alpha.-KTx, a pos. charged side chain, possibly a Lys, interacts electrostatically with ions residing inside the Shaker pore, and (b) a part of the toxin occupies an externally accessible K<sup>+</sup> binding site, decreasing the degree of pore occupancy by permeant ions. The authors conclude that, although evolutionarily distant to scorpion toxins, .kappa.-PVIIA shares with them a remarkably similar mechanism of inhibition of K channels.

IT 196605-79-5, .kappa.-Conotoxin-PVIIA

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(neurotoxin of marine snail shares with scorpion toxins a convergent mechanism of blockade on the pore of voltage-gated K (potassium)



channels)

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:477425 CAPLUS

DOCUMENT NUMBER: 131:253553

TITLE: The block of Shaker K<sup>+</sup> channels by .kappa.-conotoxin PVIIA is state dependent

AUTHOR(S): Terlau, Heinrich; Boccaccio, Anna; Olivera, Baldomero M.; Conti, Franco

CORPORATE SOURCE: Max-Planck-Institut fur Experimentelle Medizin, Gottingen, 37075, Germany

SOURCE: Journal of General Physiology (1999), 114(1), 125-140  
CODEN: JGPLAD; ISSN: 0022-1295

PUBLISHER: Rockefeller University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB .kappa.-Conotoxin PVIIA is the first conotoxin known to interact with voltage-gated potassium channels by inhibiting Shaker-mediated currents. The authors studied the mechanism of inhibition and concluded that PVIIA blocks the ion pore with a 1:1 stoichiometry and that binding to open or closed channels is very different. Open-channel properties are revealed by relaxations of partial block during step depolarizations, whereas double-pulse protocols characterize the slower reequilibration of closed-channel binding. In 2.5 mM-[K]<sup>+</sup>o, the IC<sub>50</sub> rises from a tonic value of .apprx.50 to .apprx.200 nM during openings at 0 mV, and it increases e-fold for about every 40-mV increase in voltage. The change involves mainly the voltage dependence and a 20-fold increase at 0 mV of the rate of PVIIA disocn., but also a fivefold increase of the assocn. rate. PVIIA binding to Shaker .DELTA.6-46 channels lacking N-type inactivation or to wild phenotypes appears similar, but inactivation partially protects the latter from open-channel unblock. Raising [K]<sup>+</sup>o to 115 mM has little effect on open-channel binding, but increases almost 10-fold the tonic IC<sub>50</sub> of PVIIA due to a decrease by the same factor of the toxin rate of assocn. to closed channels. In analogy with charybdotoxin block, the authors attribute the acceleration of PVIIA disocn. from open channels to the voltage-dependent occupancy by K<sup>+</sup> ions of a site at the outer end of the conducting pore. The authors also argue that the occupancy of this site by external cations antagonizes on binding to closed channels, whereas the apparent competition disappears in open channels if the competing cation can move along the pore. It is concluded that PVIIA can also be a valuable tool for probing the state of ion permeation inside the pore.

IT (196605-79-5) .kappa.-Conotoxin PVIIA

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(shaker K<sup>+</sup> (potassium) channels block by .kappa.-conotoxin PVIIA is state dependent)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:276339 CAPLUS

DOCUMENT NUMBER: 129:37385

TITLE: Three-dimensional structure of .kappa.-conotoxin PVIIA, a novel potassium channel-blocking toxin from cone snails

AUTHOR(S): Savarin, Philippe; Guenneugues, Marc; Gilquin, Bernard; Lamthanh, Hung; Gasparini, Sylvanie; Zinn-Justin, Sophie; Menez, Andre

CORPORATE SOURCE: CE Saclay, Dep. Ing. Et. Proteines, CEA, Gif-sur-Yvette, 91191, Fr.

SOURCE: Biochemistry (1998), 37(16), 5407-5416

CODEN: BICHAW; ISSN: 0006-2960  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB .kappa.-Conotoxin PVIIA from the venom of *Conus purpurascens* is the first cone snail toxin that was described to block potassium channels. We synthesized chem. this toxin and showed that its disulfide bridge pattern is similar to those of .omega.- and .delta.-conotoxins. .kappa.-Conotoxin competes with radioactive .alpha.-dendrotoxin for binding to rat brain synaptosomes, confirming its capacity to bind to potassium channels; however, it behaves as a weak competitor. The three-dimensional structure of .kappa.-conotoxin PVIIA, as elucidated by NMR spectroscopy and mol. modeling, comprises two large parallel loops stabilized by a triple-stranded antiparallel .beta.-sheet and three disulfide bridges. The overall fold of .kappa.-conotoxin is similar to that of calcium channel-blocking .omega.-conotoxins but differs from those of potassium channel-blocking toxins from sea anemones, scorpions, and snakes. Local topogs. of .kappa.-conotoxin PVIIA that might account for its capacity to recognize Kvl-type potassium channels are discussed.

IT ~~196605=79-5P~~.kappa.-Conotoxin PVIIA  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(three-dimensional structure of .kappa.-conotoxin PVIIA, novel potassium channel-blocking toxin from cone snails)

L3 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:60152 CAPLUS  
DOCUMENT NUMBER: 128:137369  
TITLE: Solution structure and proposed binding mechanism of a novel potassium channel toxin .kappa.-conotoxin PVIIA  
AUTHOR(S): Scanlonl, Martin J.; Naranjo, David; Thomas, Linda; Alewood, Paul F.; Lewis, Richard J.; Craik, David J.  
CORPORATE SOURCE: Centre for Drug Design, University of Queensland, St. Lucia, 4072, Australia  
SOURCE: Structure (London) (1997), 5(12), 1585-1597  
CODEN: STRUE6; ISSN: 0969-2126  
PUBLISHER: Current Biology Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The three-dimensional structure of PVIIA resembles the triple-stranded .beta. sheet/cystine-knot motif formed by a no. of toxic and inhibitory peptides. Subtle structural differences, predominantly in loops 2 and 4, are obsd. between PVIIA and other conotoxins with similar structural frameworks, however. Electrophysiol. binding data suggest that PVIIA blocks channel currents by binding in a voltage-sensitive manner to the external vestibule and occluding the pore. Comparison of the electrostatic surface of PVIIA with that of the well-characterized potassium channel blocker charybdotoxin suggests a likely binding orientation for PVIIA. Although the structure of PVIIA is considerably different to that of the .alpha.K scorpion toxins, it has a similar mechanism of channel blockade. On the basis of a comparison of the structures of PVIIA and charybdotoxin, we suggest that Lys19 of PVIIA is the residue which is responsible for phys. occluding the pore of the potassium channel.

IT ~~196605=79-5~~.kappa.-Conotoxin PVIIA  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(soln. structure and potassium channel blocking activity of .kappa.-conotoxin PVIIA)

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:39008 CAPLUS  
DOCUMENT NUMBER: 128:111749  
TITLE: .kappa.-Conotoxin PVIIA is a peptide inhibiting the

AUTHOR(S): Shaker K<sup>+</sup> channel  
Shon, Ki-Joon; Stocker, Martin; Terlau, Heinrich;  
Stuhmer, Walter; Jacobsen, Richard; Walker, Craig;  
Grilley, Michelle; Watkins, Maren; Hillyard, David R.;  
Gray, William R.; Olivera, Baldomero M.  
CORPORATE SOURCE: Department of Physiology and Biophysics, Case Western  
Reserve University, Cleveland, OH, 44106, USA  
SOURCE: Journal of Biological Chemistry (1998), 273(1), 33-38  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular  
Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB .kappa.-Conotoxin PVIIA (.kappa.-PVIIA), a 27-amino acid toxin from *Conus purpurascens* venom that inhibits the Shaker potassium channel, was chem. synthesized in a biol. active form. The disulfide connectivity of the peptide was detd. This is the first *Conus* peptide known to target K<sup>+</sup> channels. Although the Shaker K<sup>+</sup> channel is sensitive to .kappa.-PVIIA, the rat brain Kv1.1 subtype is resistant. Chimeras between Shaker and the Kv1.1 K<sup>+</sup> channels were constructed and expressed in *Xenopus* oocytes. Only channels contg. the putative pore-forming region between the fifth and sixth transmembrane domains of Shaker retained toxin sensitivity, indicating that the toxin target site is in this region of the channel. Evidence is presented that .kappa.-PVIIA interacts with the external tetraethyl-ammonium binding site on the Shaker channel. Although both .kappa.-PVIIA and charybdotoxin inhibit the Shaker channel, they must interact differently. The F425G Shaker mutation increases charybdotoxin affinity by 3 orders of magnitude but abolishes .kappa.-PVIIA sensitivity. The precursor sequence of .kappa.-PVIIA was deduced from a cDNA clone, revealing a prepropeptide comprising 72 amino acids. The N-terminal region of the .kappa.-PVIIA prepropeptide exhibits striking homol. to the .omega.-, .mu.O-, and .delta.-conotoxins. Thus, at least four pharmacol. distinct superfamilies of *Conus* peptides belong to the same "O" superfamily, with the .omega.- and .kappa.-conotoxins forming one branch, and the .delta.- and .mu.O-conotoxins forming a second major branch.

IT ~~196605-79-5P~~ .kappa.-Conotoxin PVIIA  
RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation)  
(.kappa.-Conotoxin PVIIA inhibition of Shaker K<sup>+</sup> channel)

L3 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:640695 CAPLUS  
DOCUMENT NUMBER: 127:274085  
TITLE: Conotoxin peptide PVIIa  
INVENTOR(S): Terlau, Heinrich; Shon, Ki-Joon; Grilley, Michelle M.;  
Olivera, Baldomero M.  
PATENT ASSIGNEE(S): University of Utah Research Foundation, USA  
SOURCE: PCT Int. Appl., 29 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734925	A1	19970925	WO 1997-US3483	19970314
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5672682	A	19970930	US 1996-619936	19960318
CA 2248710	AA	19970925	CA 1997-2248710	19970314
AU 9720690	A1	19971010	AU 1997-20690	19970314
AU 724408	B2	20000921		
EP 922055	A1	19990616	EP 1997-908897	19970314

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI

JP 2001500474 T2 20010116 JP 1997-533505 19970314  
PRIORITY APPLN. INFO.: US 1996-619936 A 19960318  
WO 1997-US3483 W 19970314

AB A new peptide, .kappa.-conotoxin PVIIA, is disclosed. This peptide is found naturally in the cone snail *Conus purpurascens* and has the amino acid sequence Cys-Arg-Ile-Xaa-Asn-Gln-Lys-Cys-Phe-Gln-His-Leu-Asp-Asp-Cys-Cys-Ser-Arg-Lys-Cys-Asn-Arg-Phe-Asn-Lys-Cys-Val where Xaa represents 4-trans-hydroxyproline, hydroxyproline or proline. This peptide together with a previously disclosed peptide, .delta.-conotoxin PVIA, act synergistically to rapidly immobilize fish which are injected with the two peptides. Injection of .kappa.-conotoxin PVIIA alone results in different symptoms with an injected fish becoming hyperactive and then contracting and suddenly extending all major fins. This fin-popping occurs repeatedly resulting in a series of jerky movements, but injection of only .kappa.-conotoxin PVIIA does not immobilize or kill the fish.

IT **196605-79-5P,** .kappa.-Conotoxin P VIIA

RL: ADV (Adverse effect, including toxicity); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation) (conotoxin peptide PVIIa)

FILE 'HOME' ENTERED AT 08:40:31 ON 15 JAN 2003